Section of Psychiatry

President Noel Harris MD

Meeting October 11 1960

President's Address

The Prevention of Mental Stress and Disorder [*Abridged*]

by Noel Harris MD (*Wiveliscombe, Somerset*)

Unless the ætiology of a disease is known it is not possible to give any precise instructions as to how that disease can be prevented. Unfortunately this applies to a considerable extent to psychological medicine. Past and present literature gives us little help. In this paper the three main categories of mental disorder will be dealt with in turn.

Amentia

Until quite recently little was known about possible means of preventing a woman from giving birth to a mentally defective child. I do not regard the treatment of a cretin with thyroid as a prophylactic measure; that comes within the realm of treatment not of prophylaxis. Recently, however, research work carried out by a number of different workers has stimulated considerable interest in the prevention of mental deficiency, although it is early to claim too much. This research seems to be developing in three directions. There has been some recent work in chromosomes which may represent a real step forward in the understanding of the production of some types of mental deficiency. Up to the present it has not been possible to utilize this knowledge practically, but it seems pretty certain that it will lead to valuable knowledge of the way in which the chromosomes may determine the development of inherited characteristics. With the knowledge of chromosome structure and its effect, it may become possible to use it clinically.

Another interesting genetical advance is the discovery that it is possible to diagnose apparently healthy carriers of recessive genes by biochemical stress. This has been possible in the case of phenylketonuria, and in galactosæmia when a galactose tolerance test has been found slightly subnormal. Abnormalities in apparently healthy carriers of Wilson's disease (heterozygotes) have been shown to have disturbances of cæruloplasmin. The ability to recognize normal heterozygotes might at least help in the prediction of the likelihood of abnormal children being born to a man or woman.

Moreover, the better understanding of the metabolic structure in some of the disorders can lead to the development of methods of treatment. Phenylketonuria is an example of this and the results of phenylanaline-free diets have been reported.

This new field of work has just been summarized by Moncrieff (1960). This work raises hope for our attaining further knowledge and clinical ability in the prevention of some types of amentia.

Psychoses

Here our knowledge is even less. At the present time there is little or nothing that can be done to prevent the onset of the manic-depressive nor schizophrenic psychoses. The incidence of the acute confusional psychoses has probably been lessened by improved conditions of life, modern hygiene in association with childbirth, and the introduction of the antibiotics and penicillin in the treatment of sepsis at an early stage.

The earlier and better treatment of syphilis seems to have lessened the number of patients who develop general paralysis of the insane.

The care of the aged has improved greatly and this may have prevented the onset of senile disorders to a certain extent, but here again it is probably treatment rather than prophylactic measures which has made the advance.

Neuroses

In the neuroses the position is rather different, and there would appear to be more opportunity for adopting prophylactic measures.

There is still no unanimous opinion concerning the ætiology of the neuroses, but there is much evidence and general agreement that many of the illnesses coming under the diagnostic label of the term neuroses are caused by emotional stress produced during the early upbringing of the child, especially during the first seven years of life.

The evidence brought forward by child guidance clinics, and from the experience of those who have specialized in the 'mental' health of children is very considerable. Even so, many points of disagreement still exist amongst pædiatricians, educationalists and others working with, and for, children.

As an example of such disagreement consider how frequently the old problem crops up of whether the behaviour of a child or adult is due to some physical cause, or some psychological cause. The question may arise of culpability and whether a person has control over his actions. If there is sufficient evidence that the neuroses may be caused by emotional stress in the first seven years of life, then education of the public in this fact, and how to bring up children in such a manner as to prevent emotional stress is essential.

If we are going to attempt to educate the public we must so far as possible present a united front.

I wish to make the strongest possible plea that members of our own profession, and especially those specializing in psychological medicine, should do all in their power to avoid biased or bitter disagreement. Constructive criticism is essential to, and helpful in, research work, and produces progress in knowledge. There is all the difference in the world between such criticism and the sort of letter or article which is still seen in the professional and public Press, which only encourages the public to distrust the work that is being done by psychiatrists and others. Some of you may feel 'what does it matter what the public and lay Press think about us?' I believe it does matter because, as I hope to show, if prophylaxis of mental disorder and stress is going to be carried out successfully the public must feel confident that the advice they are being given is sound, based upon experience and generally agreed upon by the medical profession.

It may be a long time before our knowledge of the causation of all forms of mental disorder is so accurate that definite statements can be made, as, for instance, they can in the prevention of malaria. On the other hand it is almost certain that a great deal of prevention can be carried out if the public become convinced that it is worth while. This suggestion that a greater attempt be made to educate the public in these matters, brings up another thorny problem.

In his Presidential Address to this Section in 1951, Dr Desmond Curran (1952) raised the point 'where should a halt be called in an expansionist campaign'. He wisely pointed out that psychologists could do harm to their specialty by pushing forward their views without adequate proof that such views were correct.

I doubt if the stress of the world can be lessened without the world getting a greater knowledge of psychology. Medical men have a basic knowledge of the anatomy and physiology of the body and those of them who in addition have studied the subject of psychology should be better qualified than others to express an opinion on the phenomena of animal and human behaviour. Others studying psychology may perhaps have much more theoretical and practical knowledge of the development of intellect, but less to do with managing problems of behaviour and emotion.

Perhaps, therefore, there is some justification for thinking that we can and should attempt to express our beliefs in public, and enter a field that may appear to be not purely medical.

If we are going to attempt this I am certain that we have got to do it with considerable diffidence and not be afraid of saying 'I don't know'. We must not dogmatize unless certain of the truth.

In considering this question of whether psychiatrists should try to educate the public even if it brings us up against them it is helpful to study the history of the public health authorities.

The Society of Medical Officers of Health feels that it is the duty of the whole medical profession to educate the general public in healthy living.

Take two examples: Statistics show that there has been a considerable fall in the proportions of deaths of mothers in childbirth and in young babies as the result of pre-natal care, skilled delivery of the baby and post-natal care of the mother and baby. This has been largely brought about by local health authorities, maternity clinics and units all working with general practitioner obstetricians. It has meant education of the public and it is pretty certain that some of the pioneers in this work could tell us of the bias and opposition which they came up against.

A second example is the great reduction in deaths from pulmonary tuberculosis as a result of public health education, improved housing and ventilation, more satisfactory hygiene, such as the anti-spitting campaigns, better nutrition and the discovery of active cases by mass miniature X-ray.

The result of all these activities is that there are less than 4,000 deaths from tuberculosis a year.

All this work together with BCG vaccination of babies and young persons would not have been possible without convincing the general public of their value and so getting their co-operation.

In the past, far more attention has been paid to educating the public in healthy ways of living from the physical point of view than from the mental; not enough has been done to try and educate the public in mental health.

Splendid work has been done and is still being done by such organizations as the National Association for Mental Health. The fact remains, however, that the education of the public in mental health matters lags far behind. It is the

experience of most of us that the average individual is only too ready to express his view on the topic of mental health, and even more the reasons for people's behaviour without having made any serious study of what really does influence behaviour, or even to obtain all the facts in some particular case. A common example of this is the way the public dogmatize about delinquency without having the remotest idea of what facts are known about this extremely difficult subject.

Another problem that needs consideration is whether the scientific advances that have been made in recent years do cause harmful mental stress or not. There has been the splitting of the atom, the production of the hydrogen bomb, the increase in high speed and altitude flying, the increased power and speed in motor cars and the development of automation.

In his Presidential Address to the Chemistry Section of the British Association (1960), Dr James Taylor is reported in the daily press to have said, 'The painted savage wants more food in his belly than his brothers, Mrs Jones wants a bigger ice-box than Mrs Thomas, Mr Khruschev wants a bigger I.C.B.M. than Mr Eisenhower. That's how it is. Competition is the flowering of the law of survival. Individuals, families, organized groups, countries and nations all compete for a living from restricted resources', and after expressing the opinion that the people of Britain have never been so well off he adds a warning that our position is precarious and that we should need all the help that scientists could give us! I wonder if he had in mind those scientists who are studying how human individuals are going to be able to adjust themselves to such advances, and whether they can do it gradually by a process of evolution, or whether they need every possible help to obtain knowledge of how to use their advances?

It is impossible not to be worried by the stress resulting from the impact of competition between nations and their behaviour in many parts of the world to-day. Conflict and frustration is set up in people's minds over the apparent contrariness of the behaviour of people. For example, on the one hand the behaviour of Russia gives rise to fear, anger and justifiable indignation while on the other hand such a report as that written by Dr J H Hunt and published recently in the *Sunday Times* allays that fear and produces respect. In a personal communication from Dr Philip Hopkins, for which I am grateful, he states that the Soviet Medical Service is based on the simple fact that it is easier to prevent than to cure illness, and much of what he writes indicates a most progressive attitude that can only be praised and admired.

Common sense suggests that all these facts do indeed cause mental stress and that, from these, emotional disturbances arise which are sufficient to cause illness in the form of an anxiety neurosis, or one of the forms of psychosomatic disorders.

Yet there is evidence that if the innate make-up and/or the early upbringing of the child is psychologically correct then the stress in the world to-day will not cause a mental disorder in such a person.

Again there appears to be evidence that the stress of the world to-day will not always produce mental disorder in a person even though their upbringing in childhood may have been very bad.

Is it possible that when a situation arises which threatens human self-preservation and frustrates action, that it is then that mental disorders occur? The hydrogen bomb and other modern missiles might create such a situation. Also considering the reproductive realm, is it such a situation as has arisen in some of the larger cities – over-crowding and poverty with little or no outlet for art, music, and all the creative side of life combined with the great difficulties of satisfying the sexual feelings and production of children under such conditions – is it this type of problem rather than world conflict which causes the stress leading to ill health?

Can man adapt himself to any degree of emotional disturbance if his innate make-up is sound?

It does seem to be particularly apt that at this time we should ask ourselves what, in all this conglomeration of facts, are the most important ones in causing illness. These problems are so fundamental that it would seem to be our duty to put them before the public, to answer them as best we can, and to emphasize the importance of research in trying to solve them.

I have posed many questions to you. What practical suggestions is it possible to put forward?

I believe the most important immediate action is to concentrate on attaining the best character formation in children; and here by character formation I mean the greatest degree of ability to adapt successfully to life.

I do not believe that successful adaptation to life consists in obtaining great wealth, or power, or status, but rather in being able to live up to a certain standard of ideals, get on with and adapt oneself to other people and one's environment.

This means more research to find out the best way of bringing up children – it is not a wholesale job, it is individual work. Also it means education of the public on the best and safest methods. This is not going to be easy. However, I was interested to read in the *Daily Telegraph* the remarks made by Professor E. M. Backett in which he urges the revolutionary change that a doctor should devote at least 50% of his work to healthy people from the prophylactic point of view. He felt that some doctors considered they should not meddle in their patients' mode of livelihood and said that if the new general practitioner is to take his job

seriously he must meddle, and his meddling must be increasingly personal. He must be prepared to make himself a damned nuisance to his patients.

If Professor Backett is right and the medical profession is going to do more then they have got to be taught and trained how to do so. It is only recently that the teaching of applied psychology to medical students has been undertaken. There is great necessity to stress more and more to medical students the need for understanding human relationships, and training them to be able to make the best possible relationship with their patients. The teachers must set an example in clinical work. This teaching on human relationships can very well be related to the teaching of the principles of public health, and methods of prophylaxis.

In the postgraduate study of psychiatry more attention should be given to semantics. It is unfortunate that psychiatrists frequently use words in common everyday use which, for them, have a special technical meaning differing from the meaning conveyed to the public by that word. Moreover, the public are beginning to use psychiatric terms in the wrong sense, all of which leads to misunderstanding. For example, there was a large heading recently in an excellent daily paper 'Schizophrenia at the T.U.C.' I was glad to read a report of the remarks made by Dr Eric Strauss at the conference of the British Medical Association (1960) stressing the importance of 'talking and writing a language we all understand'.

The Royal Medico-Psychological Association would render a great service to our profession and the public if they instituted a conference with other associations interested in semantics and put forward suggestions for simplifying and clarifying our terminology. Individually we can all pay particular attention to the use of the words we use, especially when lecturing or writing.

There has been a steady increase in the amount of research work carried out in psychological medicine over the past forty years. I think that much more should be done to encourage research, not only the research of a team working in a unit, but individual work. If every medical officer in hospitals was encouraged to pay more attention to the observation of 'the unusual symptom or happening' and greater opportunities made for correlating such observations from all over the world, I feel that some revealing truths might be found, or indications for a line of research be shown which a team could follow through.

There should be closer correlation between those doing research work on physical factors, such as what determines personality types, and those doing research in deep psychological realms, such as the significance of Jung's concept of archetypes.

More active co-operation with such bodies as the NSPCC and any of the associations representing parents might provide further knowledge.

Recently I wanted to find out if children who had come from very unhappy broken homes ever seemed to show no ill-effect at all so that I could try to assess some of the points that I have already mentioned, and the Rev Arthur Morton, Secretary of the NSPCC very kindly furnished me with a number of examples. Here is a chance of further research – why do some children seem not to be affected by awful home conditions in the first few years of life?

I believe that the RMPA might establish a central research bureau where correlations of individual's observations could be carried out.

The fact remains that if we are going to be successful in educating the public and in preventing the neuroses, including psychosomatic disorders, then we must be able to give them facts and not just theories and we must not dogmatize unless we are sure.

In the last three years there has been development through the co-operation of the RMPA and the Society of Medical Officers of Health. The Society has instituted a Mental Health Section and is becoming well aware of the great work that there is to be done in connexion with the new Mental Health Act.

It is to be greatly hoped that the Medical Officers of Health will become convinced of the importance of establishing the mental health of the nation, that they will work in co-operation with psychiatrists, will help to develop research and to educate the public. Where this is being done it seems to be showing good results.

Medical Officers of Health can do a great work in helping forward co-operation with educational authorities. I feel that many people teaching in schools think too much of their job as being development of the intellect in children, and not enough of the importance of character formation. How many school teachers have had the opportunity of learning any modern psychology? Do they find it of any help in the training of character? There should be the closest relationship between the parents and those who are teaching the children in school. Opportunities for the relationship must be made.

The Child Psychiatry Section of the RMPA in some of their valuable reports have stressed much of what I have said but I believe that it needs repeating and acting upon.

To attempt to give a child the best character with which to cope successfully with modern life and future eventualities is not going to be an easy task and will mean a good deal of sacrifice and hard work on the part of the public. At times it becomes wearisome for parents and others so there is a tendency to turn away from hard work,

and from listening to those who advocate it.

Where there are differences of opinion between school authorities, child guidance clinics, psychologists and those working in education, I feel sure that the Medical Officers of Health can play an important part in helping to smooth out difficulties. If a real attempt is going to be made to educate the public in these matters it is surely essential that the help of the public Press is obtained. Up to the present time the attitude of the Press to mental health has not always been very helpful. It is quite understandable that the Press want to sell their papers, that they want to encourage the public to buy and so they use all the natural tricks of the trade to arouse in their public the curiosity and interest which will attract them to buy. On the other hand it is possible that harm can be done by giving the wrong impression or information, or by arousing the feelings of the public through the force of suggestion or ridicule, or one of the many ways in which reporters are such adepts.

It may have been noticed that in this Address I have quoted what a number of people are reported to have said. I did this deliberately taking the reports from the daily Press rather than adopting the more orthodox method of using solely the medical press in order to try and show how the public get information about these matters.

I have noticed the following headlines in four papers recently: 'Crime wave reaches new and more violent peak.' 'Lie detector intrigues scientists.' 'Delinquency not "disease".' 'No frontier for delinquency.'

After such a collection it might do real good if the paper responsible would publish a serious article, as one or two of them do, giving the medical views that are as near the truth as is known at the time. For instance, take the question of delinquency which is so much in the public mind at present. I imagine that a majority would agree that delinquency is not a disease. Agreement would probably be reached on saying that the behaviour which we designate by the term may be seen in a number of different types, viz: the psychopathic personality; in epileptic automatism; a small number of aments; rarely, someone with no organic disease, but suffering from a deep seated psychological disturbance. The plain 'bad' man who, having no organic or psychogenic illness, has quite consciously decided to behave in such a manner. If the Press could help the public and the law to accept that this is accurate knowledge though incomplete, something would be achieved.

It may be necessary to change to some extent the policy of the medical profession towards publications in the Press. While the present attitude of the profession towards advertising or self gain through writing in the Press must obviously be upheld as firmly as possible, it should be possible to supply information and articles to the Press through certain bodies, as the British Medical Association already does.

Professor John Cohen is reported to have spoken to the Psychology Section of the British Association on the present developments in producing robots and other automata. Can reports and stories of such developments, unless very carefully written, give rise in children's minds to the idea or fantasy of such achievements being associated with a sinister power and evil?

It seems as if the time may be coming when such bodies as the British Medical Association, the National Association for Mental Health, the Society of Medical Officers of Health, and the Royal Medico-Psychological Association should invite the appropriate representatives of the Press to a conference to discuss the whole matter.

Much of what has been said about the Press applies equally to sound broadcasting and television. They can, I believe be used much more to help forward the cause of mental hygiene.

It is obvious that such a policy as I have outlined is going to cost money. Where can this money be raised? Munificent gifts are still being made by individuals and the very wealthy Trust Funds founded through individual generosity. Ever since I started to think about this Address, gifts which I had never believed possible have been announced. I am particularly thinking of the sum raised for investigation into the causes of and care of 'spastic' children.

Then there is the £23,000 grant from the Ford Foundation for Fellowships at the Institute of Criminology at Cambridge University, also the £25,300 given by the Nuffield Provincial Hospitals Trust to Political and Economic Planning for a study of the mental health services. But it would be impracticable to expect all the money necessary to be raised from such sources.

At the present time the amount of money being spent by our own and other nations on scientific research is colossal, and a large proportion of it is going into the production of the most efficient hostile missiles for the purpose of keeping peace by the threat of being the most powerful nation in war! Great Britain, the United States of America and Russia must be spending many hundreds of millions of pounds for such purposes.

Recently in the public Press the following announcement appeared: 'France plans to spend an extra £842 million in the next five years on equipping her armies with nuclear weapons and the means to deliver them. This brings total military expenditure for the five years to £3,220 million.'

In contrast, consider these announcements: 'Britain's youth services are to benefit by a further £4 million Government Grant to be made avail-

able in the period 1962–64. This follows the £3 million grant for the 1960–62 period announced after the publication of the Albemarle report.' 'Government's £46,000 aid to youth work. This sum was made for special experiments in youth service and is to be shared by four organizations in the next three years.'

What are these sums of roughly £7 to 8 millions expended by the British Government in comparison with what is being spent on atomic research, ballistic missiles and such activities? Nor does there appear to be much mention in the policy of governments of the prevention of mental disorder. The National Association of Local Education Authority Youth Leaders is said to have asked the Government for £50 million for a plan connected with youth clubs, but will they get it?

Considering all these facts makes people wonder whether the time has not come when it is essential for the people of the world as a whole to reconsider the ideology for which we must aim. Air travel is bringing us so close together that the world can no longer think of itself as widely separate units. The world is rapidly drawing together as one large family. Constant rows in a large family generally cause it to disintegrate pretty quickly. Surely we must ask ourselves if the advances in the world to-day which should bring benefit to all are in danger of bringing disaster because intellectual development is outstripping character formation.

If there is the slightest danger of this, then those of us whose object in life has been the care of the body and the mind must express our opinions on preventive measures.

Every effort should be made to emphasize the importance of research work. It may become infinitely more important to spend millions on endeavouring to find out more about the human mind, its unconscious life, its emotions and influence on behaviour, than to continue to spend money in other directions.

More attention must be drawn to the need to find out the best means by which individuals can adapt themselves to life. Perhaps I have irritated some of you by my use of the term character formation, which, I must admit, does smack of 'morals' in a form which we have rightly been up against in the past, but I have deliberately used such a simple term as I felt it denoted what I meant. I have also spoken of the importance of obtaining, as nearly as possible, a unanimous opinion which can be presented to the public. Can it be said, for instance, that for a child to develop the best possible adaptation to life he must be able to satisfy his instinctive drives according to his age and that repression and frustration of these drives must be avoided as much as possible; also that from the earliest years a sense of self-discipline must be inculcated which includes getting pleasures and satisfaction without them being at the cost of other people?

In considering this wide vista which I have brought before you to-night it is essential to consider the activities of the Church. Christianity above all else should stand for the best possible type of human life, and should set the highest ideals. Yet there has been, and still is, much disagreement between psychological teaching and theology. But has sufficient attention been given to straightening out such disagreements?

There are such groups as the Churches' Council of Healing, and the Guild of Pastoral Psychology who are anxious to co-operate in the treatment of the sick, and have done much to help forward the greater understanding of what is known about human behaviour through modern psychology, and what has been taught by the Church.

It is, I think, fair to ask how much work is being done by the Churches on the question of human behaviour, and what impact they are making on adolescents throughout the world.

Surely the one thing the Church should not be afraid of is seeking after the truth. Therefore, much greater efforts should be made to find out if the Churches are exerting the influence for peace, security and love which might be expected.

The Bishop of Blackburn was reported as saying a short while back that it seemed a great pity that Christians should be debarred from worshipping together. If there cannot be common agreement in theory, surely there can be on behaviour? Much of what psychologists are aiming at is similar to the ideal behaviour as laid down in the Bible, for instance, in the Sermon on the Mount.

What is, I believe, a pioneer course has just been started in the Exeter Diocese with the approval and full co-operation of the Bishop. A course of lectures on applied psychology is being given to the Church of England clergy working in the Diocese and any medical men who wish can attend. The lecture is followed by questions and discussion, the whole lasting about two and a half hours. These lectures will probably be followed up by discussion groups in various parts of the Diocese, which is a large one. Such co-operation may well lead to increased knowledge and the introduction of preventive measures.

I have dealt with my subject by considering a large area of life, but the incidence of disorders resulting from emotional upset including as it does the large number of psychosomatic illnesses, justifies, I hope, looking into and investigating every possible avenue of approach in order to find a means of prevention.

REFERENCE

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Section of Laryngology

President J H Otty FRCSED

Meeting November 4 1960

President's Address

Retrospect and Prospect: A review of the Training of Otolaryngologists in Great Britain

by J H Otty FRCSED (*Bradford*)

In choosing this subject I have been influenced by what seems to me a serious situation. Some few years ago there appeared to be too many candidates for too few consultant posts, a situation that no longer obtains. In addition a number of my younger colleagues have suggested that I discuss the training of specialists in this country. My intention is to look at the position of our specialty as it was, as it is now, and how I think it should develop.

We received recognition relatively late in this country. Cann (1958), in his Presidential Address, pointed out that the early laryngologists were physicians – a notable exception being Sir Henry Butlin, a general surgeon who was persuaded to take up laryngology, which no one else was keen to do. In many cases the Ear, Nose and Throat Departments were given into the charge of surgeons who in some cases had little real interest. These men were given charge of a very small number of beds and for many years the major part of the work was done in the outpatient department. Nearly all tonsil cases, and many nasal operation cases also, went home the same day as their operations. Such beds as were allotted were largely filled with acute mastoid patients, who frequently spent many weeks in hospital. As a result we have been looked upon as practising a minor specialty and I fear that in many places we are still not accepted as equals by our surgical brethren. The work largely consisted of removal of tonsils and adenoids, operations on the nose and sinuses and the treatment of acute and chronic mastoiditis. Malignant disease was usually handed over to the general surgeons, and in Scotland one of the foremost exponents of laryngectomy was better known as a genito-urinary surgeon. In many places otolaryngology and ophthalmology were practised by the same man and this obtained in many provincial centres up to the inception of the National Health Service. Some of the earlier surgeons maintained their interest in general surgery by dissection of tuberculous glands of the neck and dealing with enlarged thyroids, but for many I feel it was too easy to earn a very comfortable living by removing tonsils and adenoids, excising the anterior ends of middle turbinals, doing a submucous resection of the septum and the occasional simple mastoid operation. At that time there was little postgraduate instruction to be had in this country and those who were interested made the pilgrimage to Vienna where there were facilities for such training.

As a medical student I learnt little of the specialty – ten weekly lectures and one weekly attendance at outpatients over the ten-week period were the requirements. An oral examination – largely farcical – was conducted at the end of the term – I do not think anyone ever failed to get 'signed up'. I saw no E.N.T. operations till after I qualified and my first introduction to them was on a Saturday morning four days after my arrival to take up my first house surgeon post, when I was called in to anæsthetize 35 cases of tonsils and adenoids, performed by the senior house surgeon. I can still see the outpatient waiting hall, the forms put together and covered with mattresses to accommodate the unfortunate children. A somewhat similar performance took place when I came to London in 1929, though the numbers were fewer.

All this is thirty years ago, but I fear that even

to-day we have received little more recognition from the powers that select the curriculum for the present-day medical student. Miss Collier dealt with this in her Presidential Address (1955). The amount of instruction varies enormously. In some cases the students attend 'if they wish'. In other cases they must because they have an examination at the end of their period of instruction and also a question in the final examination. There is no uniformity. Recognition of our subject in the final examination seems to me to be the crux of the problem. The student of to-day is so over-burdened with subjects that only if he fears he may have a question in his finals will he make time to study our particular one.

I would like to see a wholesale pruning of the medical curriculum, but that is another matter. Miss Collier rightly points out that we can make a very definite contribution to the education of potential doctors. The taking of a concise and accurate history is important if an accurate diagnosis is to be made and this must be followed by precise observation and accurate description of what is seen. In rhinolaryngology especially, the patient has to be considered as a whole; many of the conditions which demand our attention are not purely local lesions, but manifestations of general systemic disorders. I feel sure that the day of the special hospital is past. It is no longer possible, for the good of our patients, to work in isolation. We need the help of all the resources that can only be found in a large general hospital. Hence I view with some apprehension the continued expansion of the only centre for post-graduate training in our specialty in this country in connexion with a purely special hospital.

In 1945 the Ministry of Health published the results of a hospital survey for the whole country. In connexion with the services in Yorkshire one recommendation of the Surveyors reads: 'We are of the opinion that, in view of the necessity for an increase in post-graduate centres for the training of specialists, that Leeds should confine itself to undergraduate teaching and that the Bradford Royal Infirmary should be made a centre for post-graduate education'. This, of course, has not happened – indeed I wonder how many of the recommendations of these hospital Surveyors have ever been implemented, especially those dealing with postgraduate education. One recommendation is, I am happy to say, about to be realized – that the Royal Eye and Ear Hospital in Bradford should be rebuilt as an integral part of the new hospital – on the Royal Infirmary site.

In a report on postgraduate medical education and specialist training published by the World Medical Association in 1950 enquiry revealed that in many countries there is a great need for more specialists and further that there are few, or none, of the facilities for producing them. This country was reported to have inadequate representation of specialists in all fields and the facilities for postgraduate education were not wholly adequate. In reply to the question, 'Is the training programme of specialists adequate', the reply given was, 'There is no general and specific programme for the training of specialists'. Many members of the medical profession deplore the multiplicity of diplomas in special subjects, many of which are of recent establishment, because it tends to divide into watertight compartments the art and science of medicine. Such a division, if carried too far, encourages the labelling of a patient's illness as a particular disease or a disturbance of a particular organ or part of the body and discourages the care and treatment of the patient as an indivisible whole.

It was said that the relative failure of Great Britain in the recent Olympic Games was due to a lack of training facilities. I wonder if this is not true in our specialty. Talking with a colleague some time ago I suggested that we were becoming imitators rather than initiators. He agreed and said he had heard the same opinion expressed elsewhere. Is this true, and if so why is it true, and what can be done to remedy it? I believe that it is true.

Prior to the inception of the National Health Service, while a specialist spent a good deal of his working time in hospital he received no remuneration therefrom and of necessity he had to take on numerous hospital appointments to give him connexions with as many general practitioners as possible in order that he might build up a private practice. As this practice grew he shed the less attractive and less remunerative appointments and devoted more of his time to the larger hospitals. Here, however, he was usually short staffed and overworked and in many cases he had little time to devote to teaching residents. He was grateful if they could take some of the routine work off his hands. If he had the time and the inclination for research he probably had to finance the whole project himself and even in University centres it was, and is, far from easy to get financial assistance for any project outside the university departments.

To-day there are more consultant posts and throughout the country more beds for the specialty than ever before, but the pressure on the individual is the same, or greater, in spite of his being relieved to a very large extent of any financial worry. Regional Boards and Management Committees are for the most part not interested in the training of consultants. They are too preoccupied

with waiting lists and feel that it is no part of their duty to see that the consultant should devote time to the training of his registrar. They feel that it is no part of their duty to see that a man in training has time to study for a higher degree. This may not apply to all boards. Now that there is a marked scarcity of applicants for posts in the registrar grade, the Leeds Regional Board proposes to set up some posts, of the nature of rotating internships in the junior hospital medical officer grade, in the hope that thereby some may be attracted to stay on in the hospital service.

In spite of the number of consultants and the increase in the number of beds, I venture to suggest that these are not being used as well as might be. I have looked up in the Medical Register the appointments of all the members of the British Association of Laryngologists; some 300 in all and 91 others whose names I came across and who are not members of that Association: most seem to hold appointments at four hospitals, some have as many as nine, and others as few as one. In very many cases there is only one consultant E.N.T. surgeon on the staff of a hospital. I cannot myself believe that these departments are really satisfactory and I feel that, for the good of the patient and the future of the specialty, the work must be concentrated in fewer and larger departments.

I am pleased that in its recommendations to the working party on the staffing of hospitals the Central Consultants Committee of the B.M.A. view with favour the reintroduction of the old voluntary hospital nomenclature by which Consultants are either Physicians or Assistant Physicians, Surgeons or Assistant Surgeons, so long as these appellations are applied only to Consultants. The nomenclature would enable an easy definition of certain duties to be made.

The reintroduction of this firm system among other things allows for earlier security and some economy in the establishment and employment of junior staff. It seems to me that when this is done there must be real safeguards for these Assistants to ensure that after a time – say, when they reach maximum salary – they then become full Surgeons or Physicians with charge of beds.

There is evidence that registrars and senior registrars are reluctant to apply for posts away from teaching hospitals and certain other large hospitals associated with them. The reason for this reluctance is based on past experience of those who have found that such a step has seriously reduced their chances of obtaining a consultant appointment. To provide a wide experience and tc meet the needs of hospitals a period of one or two years in a regional hospital should be regarded as a desirable step towards obtaining a consultant post. It should be an obligatory part of the training period. Some safeguard is necessary to ensure that a man can look forward to having charge of beds and that what sometimes obtained in the past – a man remaining an assistant all his working life – is no longer possible. The concentration of small departments into larger units would make easier the interchange of registrars for training. The staff from the larger centres could visit a few of the more remote areas to see outpatients, but in this country, where distances are not great, inpatients should come to the larger centres. Only in this way can we hope to get adequately trained staff, both medical and nursing, and only in this way can we justify the technical staff which are becoming more and more necessary. It is only in this way that the training of future specialists can be improved and some research undertaken.

In the training of specialists in this country it seems to me unfortunate that our postgraduate school at Hammersmith has such a small E.N.T. Department. It is true that postgraduate work is done by the Royal National Throat, Nose and Ear Hospital, but some complaint is made that the courses are mainly theoretical and insufficient emphasis is given to the practical side.

I wrote to several ex-house surgeons and registrars, who now hold consultant posts, and asked them to tell me frankly wherein their early training was lacking. They all thought that their basic training was reasonably adequate except in aural surgery and endoscopy. They made a plea, which I would very strongly support, for more facilities for cadaver surgery under supervision. I hope that the working party on the staffing of hospitals when it reports will suggest that in certain hospitals – not necessarily teaching hospitals – a sufficient number of staff is provided to enable the senior members to give adequate time to the supervision of their juniors in training.

Cadaver surgery has never had much place in the training of specialists in this country. Pathologists have removed temporal bones so that some material is available, but any other work has had to be done in an almost furtive manner not encouraged by the pathologists. I would suggest that hospital authorities look at this matter realistically. Is it better that practice should be obtained on the cadaver, or on the living, with all the risks of a poor result that this entails? I am quite serious about this for I was fortunate in spending a year in an Anatomy Department with plenty of material for this practice and also in having done a good deal of cadaver surgery in Vienna. It is true that occasionally courses in temporal bone surgery are to be had in this country and, I believe, formerly in endoscopy, but

they do not cater adequately for the embryo consultant. The most recent one advertised, a course in practical aural surgery, had four and a half hours practical work on the wet temporal bone. Compare this with the requirement that an applicant must have available fifty temporal bones before he can be enrolled in one of the American postgraduate courses. I think there is a place for regular courses in all types of surgery of our specialty to be given by exponents from different centres; specialists from abroad could also take part. These courses are, I think, necessary, not only for the training of young specialists, but to acquaint established specialists with the newer techniques which are being practised in different parts of the world.

Training in endoscopy is singularly lacking in this country. One of my friends was so worried about his lack of proficiency that as soon as possible after the last war he made the pilgrimage to Philadelphia to obtain the instruction possible there. Visiting the Lempert Institute on his way home he is now known more for his aural surgery than his endoscopy!

Before the last war there was established in one of our L.C.C. hospitals a centre which was intended to be a centre for endoscopy and to deal with foreign-body cases for the Greater London Area. It is a pity that the war prevented this from maturing, since it could have proved the centre for the training in endoscopy which is so lacking in this country. Many of us owe a very real debt to the late Chevalier Jackson and his son who conducted such valuable endoscopy courses in Paris in the unit of Professor Lemaitre.

Would it not be possible for some such courses to be started in this country? It is not easy. Our Home Office regulations preclude the use of dogs to enable one to obtain experience on the living. It must be remembered that the Cruelty to Animals Act of 1876 precludes any surgeon in Britain from using an animal for the attainment of manual skill! Endoscopy is still an important part of our work, for while much is done by our colleagues in thoracic surgery, they have shown little inclination to take over the foreign-body work, hence I think the legal aspect will have to be investigated.

What can be done to raise the status of the specialty in the eyes or our colleagues and throughout the world? First, we must obtain better recognition in the universities. There are only two professorial chairs, one at Manchester and the other at the Institute, which comes under London University. I hear rumours that others are to be founded and I hope these will prove well grounded. Since much of the work of general practitioners consists in dealing with diseases of the upper air passages, surely there should be some uniformity in the requirement that our specialty should be a compulsory subject for the final examination. I suggest that it is at this stage the student's interest must be aroused if we are to recruit more men to our numbers.

Secondly, I would suggest that work be concentrated in larger centres than at present, with a minimum of fifty beds. The old attitude that anywhere is good enough for the removal of tonsils and adenoids must be eradicated. Our colleagues must be educated to the fact that we do more than they may have suspected and that, therefore, we need just as good facilities for surgery as they do. In Bradford we are fortunate in that most of our work is done in one hospital. Three tonsil sessions only are done in the Hospital for Sick Children each week. My colleagues and I visit between us six other hospitals within a radius of twenty miles to see outpatients. Some tonsil operations and minor nasal operations are done in some of these centres, but almost all the major work comes to Bradford. My colleagues in Leeds are less fortunate. They have to work in no fewer than five centres in Leeds itself and, in addition, some of them have commitments outside. Within ten miles of Leeds, and even less of Bradford, there are two towns of 150,000 people covered by one consultant who has to chase between both places to operate and to see outpatients. Surely this is far from economical and far from efficient and certainly does not lend itself to the proper training of junior staff.

Where, for geographical reasons, a man has to work mostly on his own, he should have a definite attachment to a major centre, where he can go and discuss difficult cases, or even take them for operation for the sake of the better facilities for immediate after-care. From this centre he could obtain relief in the shape of a senior registrar to act as locum to cover sickness, holidays, &c. This would be a most valuable part of the training of registrars. It is surely more economical to pay more consultants to do the work they have been trained to do, rather than to pay them to spend time motoring from one small hospital to another. To-day a man feels that once he accepts a post as a consultant he is committed to that place for life – hence the difficulty in staffing some of the unpopular areas. A friend of mine in another specialty applied for another consultant post within the same region. The outside assessor said, 'So-and-so is doing a good job where he is – there is no need for him to move' and, in spite of protests, he was not even short-listed for interview. Surely this is wrong. Some centres will naturally be larger than others and some have more amenities than others – hence I feel that opportunity must be afforded those who have proved them-

selves in a small centre to gain promotion to one of the larger and more attractive centres.

Modern equipment, both for diagnosis and treatment, is so expensive that it must be used continuously if it is to be used economically. The time is, I think, not far distant when the microscope will be used almost as much in the outpatient department as in the theatre. In addition we shall need the help of more and more technical staff in our work. Already one trade union is pressing for the recognition of deafness, allegedly due to industrial noise, to be recognized under the National Insurance Act for compensation. I think we can expect this claim to snowball. The problem, and it is one of considerable magnitude, is engaging the attention of our Association. These are further reasons why I feel there must be concentration of work.

It seems to me unlikely that the number of residents will increase in the near future. The type of resident is changing – indeed many of them are no longer resident, especially those who are attempting to become specialists. They are married, perhaps with a family, and naturally they wish to spend some time with their families. In the future hospital authorities will have to accept that residents will expect to live out most of the week and, since it is unlikely that married quarters will be provided within the hospital, some co-operation between hospital and local authorities must be brought about so that housing can be provided near the hospital. This is done in some of the Scandinavian countries with great success. They have no residents as we know them, but the staff are expected to spend their days in hospital and to cover the nights by spending one or more nights weekly in the hospital. As a result the hospital provides each resident with a bed-sitting room of his own. The latter is important for the arrangement will not work unless the man can have a place he can call his own and where he can keep some of his possessions.

If, as I have suggested, the 'firm' system comes back into hospital and the work is concentrated in larger centres, more people will be working together, instead of in isolation, as so often happens nowadays. I think this will help recruitment and, with benevolent direction from the head of the firm, better training will result. Hospital authorities must be convinced that a good return is to be obtained by a senior man supervising the work of his juniors.

I would like to see one session a week in every department set aside for research – even if that research were only a survey of one's own cases; it would prove most instructive.

The concentration of our work in larger centres should permit more research to be carried out. For example, it would be relatively easy to assess the merits of one of the new preparations that are so constantly coming on to the market if, say, two centres undertook to treat all similar cases by similar means. This would surely lead to the better assessment of the value or otherwise of a particular drug and so save us time and the Service money. There is a bottle-neck at the final stage of drug development – the clinical testing. If more doctors shared the testing of drugs at an early stage, and so assigned these more rapidly to their proper place in therapeutics, the profession might have less cause to complain of the bewildering array of new products that appear and survive on the market.

A greater investment in clinical research might well pay handsome dividends in improved health, with fewer hospital admissions and lost working days. It requires unselfishness to submerge one's individuality in group research but investigations of this type not only produce information hard to obtain by any other means, they also provide extremely valuable experience for the participants. Apart from creating a new interest, they sharpen the investigator's critical faculties in relation both to his own work and to that of others.

The attitude of the Ministry of Health seems to be that they must run this Service as cheaply as possible, not as well or as efficiently as possible. It is true that all this is going to cost money but we are going to need more and more expensive equipment and more and more technical help in the not too distant future. If the Service is to improve, this is inevitable. More money is to be made available for the building of new hospitals and those of us who will have a say in the planning of new Departments should ensure that adequate theatre accommodation is provided. More than one theatre will be necessary for such a unit as I foresee. There must be room for the investigation of difficult cases. Also there must be a room where the surgeon can sit and read and think. All too few departments have a room where a consultant can spend an hour or two reading or going quietly over his case notes. The Ministry does not feel these are essential.

How is all this staffing to be achieved? Money is not the only answer, though more will have to be found. The cry is going up to get the general practitioner into hospital but I agree with Lord Taylor (1960) who said: 'I see no future for general practitioners' beds, except in small and remote areas'. What the general practitioner needs is open access to pathology, X-ray and physiotherapy departments, a good domiciliary consultant, home nursing, home help and health visitor service at his disposal. That is not to say

that the general practitioner with special experience should not have a proper place in hospital. There are several places in this country where without some general practitioner help it would be impossible for the Service to carry on. There are some men and women who are helping in outpatients and doing most of the routine tonsil and adenoid operations. Is this a good thing? Our Association has been against the appointment of pure tonsillectomists. In any case the number of people with such experience must be diminishing since most of our residents come from overseas. I feel that if our departments were larger, if their staffs were there most of the day and were working together, some of the difficulties I have recounted would be overcome.

I think, too, that we shall have to look at the standards by which we judge a man's fitness for a consultant post.

It is laid down that a candidate for a consultant appointment should have a Fellowship of one of the Royal Colleges or a Mastership in Surgery. It is recommended in some regions that he should have this qualification if he is to be a senior registrar, but this has had to be waived in many cases. We are, I believe, the only country in the world which demands this higher qualification. In many countries there is an examination which the candidate has to pass before he is recognized as a specialist. I sometimes wonder whether we are not losing good specialists in some of those who fail to pass the FRCS examination.

The Fellowship examination is no criterion of the owner's clinical or operative capabilities. Indeed something seems to be wrong where in one recent examination of 48 successful candidates 34 were graduates of universities outside the British Isles and in another 44 out of 64 successful candidates were graduates outside the British Isles.

Are our graduates so badly trained from the beginning that only a low percentage obtain a pass, or are there so few attempting the examination, or is a deliberate effort being made to keep down the numbers with the Fellowship qualification in this country? In any case I feel that many people are going home stamped as specialists with no real training behind them and that is not a good thing.

In Austria I believe no department is recognized for the training of specialists unless it has a minimum of fifty beds. At least four years have to be spent there.

The trainees have to perform all the operations of the specialty on the cadaver, under supervision, and only if the senior is satisfied as to their capabilities are they allowed to make an incision on the living. They have to satisfy the head of the department at the end of their period of tutelage that they have performed all the operations before they are permitted to practise as specialists. The opportunities for cadaver surgery are much greater than we enjoy since in most hospitals a post-mortem examination is made on every case dying within the hospital. Ward rounds such as are held on the Continent where the whole 'firm' goes round together and where all the cases before and after operation are examined and discussed by the chief are particularly valuable.

If we are to retain the Fellowship examination as the hallmark of the specialist then surely he should sit the examination at the end of some such period of training.

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Section of General Practice

President L W Batten MRCP

Meeting October 19 1960

Valedictory Address

Dr R J F H Pinsent delivered his Valedictory Address entitled **Art and Science in General Practice**

Meeting November 16 1960

Discussion on Infectious Diseases Today

Dr G I Watson (*Guildford*)

Infectious diseases today fall into three groups: in the first the diagnosis can be made by the family doctor single-handed, such as chickenpox; in others the diagnostic physical signs are microscopic or serological, for example in glandular fever; and the third, a diminishing number of short ill-defined fevers with which the laboratory can at present give only negative assistance.

Measles: Among infectious diseases today measles plays Cinderella. Doctors may notify upwards of 20,000 cases a week, but little or no administrative action is taken on the information supplied. There is an antigenic similarity between the viruses of measles and distemper (Adams *et al.* 1958); most puppies are now vaccinated and we must all hope that measles antigen can soon be added to the infants' vaccine 'cocktail'.

Who takes measles badly? Yesterday the answer was undoubtedly 'infants under 2'. Today, without pneumonia, measles in babies is usually milder than in schoolchildren. In a survey by the College of General Practitioners (Group Report, 1957), each of 15 babies under 6 months of age had a 'mild' attack: thereafter the proportion of 'mild' measles decreased up to the age of 18–24 months, but that of 'severe' measles remained steady. Measles was mild in infants, whether the mother had had the disease or not; but breast-fed babies gained significantly in this respect over bottle-fed babies up to the age of 2 years. These results have a bearing on our use of gamma-globulin to modify the severity of measles among contacts.

Influenza: Asian influenza is still with us. Fever is of all degrees: some people have symptomless infections; in others, it is more prolonged and fluctuating. My special interest is in the M-shaped or biphasic fever pattern (Stuart-Harris *et al.* 1938) which I believe to be the reaction of a patient who has caught a second attack of 'flu' from himself before he becomes immune (Watson 1960*a*). In Fig 1 the top left hand chart shows that the girl's second rise of temperature synchronized with her mother's first bout, as if both were due to infection by the same batch of virus released by the girl two days (one incubation period) previously.

Longer serial intervals – from four to ten days – seen in some families suggest that convalescent carriers are important in the spread of influenza epidemics.

Chickenpox: Is chickenpox caught from a case of herpes zoster the same disease as that caught from another case of chickenpox? Dr Hope Simpson (1958) has been able to show that clinically and epidemiologically the diseases are indistinguishable, and I believe the two viruses have been proved identical in the laboratory (Downie 1959).

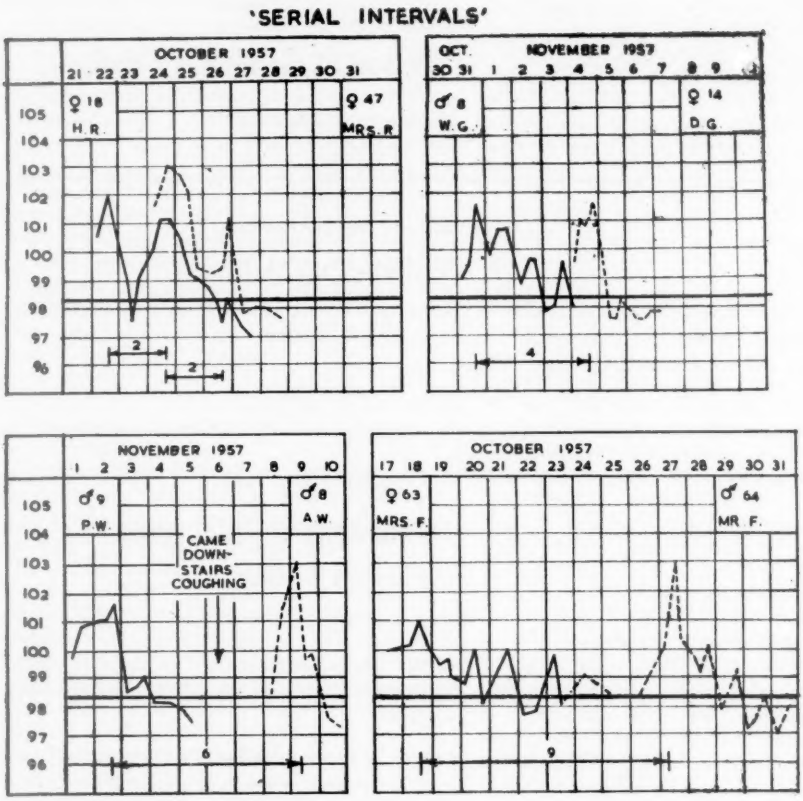

Fig 1 *Serial Intervals in Asian Influenza*

Rubella: Are there two sorts of rubella, one associated with ante-natal damage to the fœtus, the other harmless? By using Dr Hope Simpson's analytical methods we in general practice might throw further light on this problem. The incubation period of german measles is given as 17 – 18 days (Price 1947); so it is possible for a woman to be infected before she knows she is pregnant, yet miss her first period about the time her rash appears. I know of 3 mothers to whom this has happened; all 3 children have bilateral cataracts, deafness and severe heart lesions. In 2 cases the ante-natal infection was the mother's second attack of epidemic rubella. I believe that pregnant women are unduly susceptible to rubella, as they are to poliomyelitis.

Glandular fever: Glandular fever is another enigma. Here again, is this disease one or many? When the Paul Bunnell test is negative, a possible alternative diagnosis in patients with glandular enlargement and fever may be toxoplasmosis. Dr J S Robertson (1960) points to ante-natal toxoplasma infection as another cause of fœtal deformity and stillbirth, and suggests that the disease may be locally widespread, yet unrecognized.

Streptococcus pyogenes: In this antibiotic age there is a danger of thinking that bacterial infection is almost extinct. In the year from mid-August 1959, I attended 182 patients ill in bed with fever and sore throat. From 65, *Streptococcus pyogenes* of Lancefield Group A was cultured; 55 were probably due to viral causes; in 62 others, swabs were negative or not attempted. Table 1 shows the streptococcal isolations for twelve months. The aim was to study the distribution and spread of Griffith's type 12, which had only lately become common in the district. Type 1 was present in seven out of ten villages, type 12 in six, and type 6 in four. Type 12 caused two local outbreaks,

Table 1
Streptococcus pyogenes Group A
Bi-monthly Total Positive Swabs by Specific Types (Tillingbourne Valley 1959/60)

Month	*Type* 1	2	3	3/13	4	5/27/44	6	8/25	9	11	12	*Not Typed*	*Totals*
Aug/Sept	–	1	–	–	–	–	–	–	–	–	–	–	1
Oct/Nov	1	1	2	5	1	–	3	–	–	–	9	–	22
Dec/Jan	9	–	6	–	3	1	4	1	–	2	1	2	29
Feb/Mar	1	–	–	–	–	–	1	1	1	–	5	–	9
April/May	1	–	–	–	–	2	1	–	–	–	–	–	4
June/July	–	–	–	–	–	–	–	–	–	–	–	–	0
Totals	12	2	8	5	4	3	9	2	1	2	15	2	65

the first started by a child, the second by an adult. Five types caused one local outbreak each, while 5 others only occurred sporadically. Up to New Year isolations were commoner from children; thereafter adults predominated. Only types 3 and 3/13 were associated with scarlet fever; acute nephritis occurred in villages where type 12 had been isolated; types 1 and 6 were not associated with any complications and no rheumatic fever was seen during the year.

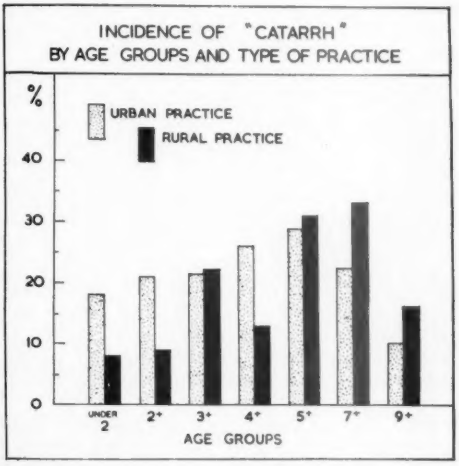

Fig 2 *'Catarrh' in urban and rural practices (3,310 patients)*

Catarrh: Fig 2, based on the measles survey by the College of General Practitioners (Group Report 1956), shows that the age distribution of children, classified by their own doctors as 'catarrhal', differed in urban and rural practices. The peak age was passed earlier in towns than in the country; in fact, 'catarrh' seemed to behave like an infectious disease, or group of infections. These are considered below.

Pyrexia of Uncertain Origin (P.U.O.): We already have ECHO or orphan viruses. We need new names for the diseases caused by viruses and to know more about their distribution. I have given details elsewhere (Watson 1959) of the benefits which follow the interchange of such information between family doctor and medical officer of health. During the year from August 1959 I attended 120 patients in bed with fever, whose illnesses did not fit the pattern of any known bacterial infection, nor respond to anti-bacterial therapy. Table 2 sets out the diagnostic labels used, showing in brackets for each group the number of cases in which laboratory confirmation was possible.

Coxsackie A and ECHO viruses: Each summer I see a small group of children with sudden onset of high fever, headache, and reddened conjunctivæ, but with no coryza, little or no sore throat,

Table 2
120 cases of P.U.O. (Tillingbourne Valley 1959/60)
(Figures in brackets = Numbers confirmed by Laboratory)

Month	*'Shere Fever' Coxsackie A*	*P.U.O. + Rash*	*Polio virus*	*Adeno-virus*	*Coxsackie B*	*'WP/60'*	*'Strep M.G.+ve pneumonia'*	*?*	*Totals*
Aug-Oct	5	5	3 (3)	3 (2)	2 (2)	–	–	5	23 (7)
Nov-Jan	–	1	1 (1)	27 (12)	–	–	–	2	31 (13)
Feb-April	–	–	–	6 (1)	–	25	–	5	36 (1)
May-July	8 (2)	1	–	8 (6)	6 (2)	–	2 (1)	5	30 (11)
Totals	13	7	4	44	8	25	2	17	120
Confirmed	(2)		(4)	(21)	(4)		(1)		(32)

nor dorsal spasm, whose illness is quickly over ('Shere Fever': Watson 1954*a*) and the laboratory confirmed it as due to infection by a type A Coxsackie virus.

Each year I also see a few cases of 'P.U.O. with rash'. Some are babies with roseola infantum but others are older children. The rash is mainly on the trunk and buttocks, like a red bird's eye with a white areola, and comes out at the end of a few days fever. Six out of seven recent cases occurred in months when I also diagnosed 'Shere Fever', and tests for Coxsackie A or ECHO viruses should be considered if multiple cases occur.

Polio virus: Two schoolchildren came back from their 1959 holiday and developed symptoms of aseptic meningitis and sore throat. Each had received two anti-polio injections six months previously. They had both recovered harmlessly from their present illness before type 1 poliovirus was recovered from their throat swabs and fæces (Watson 1960*b*). Neither parent had been immunized. Thirty-two days after the children became ill, the father succumbed with fever, severe headache, dorsal spasm and limb pain with a good deal of nasopharyngeal catarrh. Type 1 poliovirus was also recovered from his throat swab and fæces, but he too recovered at home without paralysis.

Fig 3 shows the long serial interval between these primary and secondary cases. Accepting 7 – 14 days as the incubation period of poliovirus infection (Meadows 1952), we can say that one or both children must have been excreting infective virus for 18 – 25 days from the onset of symptoms before the father was infected. This figure illustrates how the duration of infectivity can be measured, if the true incubation period of a disease is known. The success of the polio vaccine programme should not allow us to forget that anyone thus protected can nevertheless be infected with poliovirus, can suffer from poliovirus fever and act as a healthy or convalescent carrier to the detriment of the unvaccinated around him. A recently reported death underlines this danger.

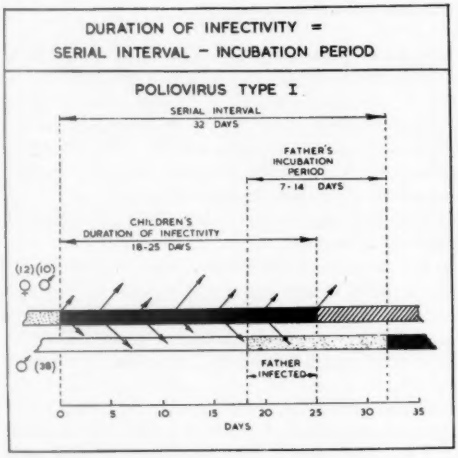

Fig 3 *Measuring the duration of infectivity*

For some years I have foreseen danger in the widespread use of antipyretic drugs to mask the symptoms of infection, particularly pre-paralytic poliovirus fever (Watson 1954*b*, 1956, 1957). Dr D S Dane, working at Professor Dick's laboratory during the 1957 polio season, was able with Dr S N Donaldson, the assistant Medical Officer of Health in Belfast at the time, to test my hypothesis by collecting data about a small series of 125 cases of confirmed poliovirus infection, relating their consumption of aspirin and other suppressive drugs to the degree of paralysis which later developed. I have permission of both these doctors to report their unpublished figures.

Table 3 shows that among non-paralytic cases nearly 80% had taken no aspirin or other tablets. Of those with not more than one limb paralysed, fewer had taken no tablets and more had taken some. Patients with severe paralysis affecting two

Table 3
Type 1 poliovirus infection
Effect of 'Aspirin &c' on degree of paralysis (Belfast 1957)

Degree of paralysis	*Amount of 'Aspirin &c' taken by each patient*					
	None		*1 – 3 tablets*		*'Many' tablets*	
	No. cases	*%*	*No. cases*	*%*	*No. cases*	*%*
None (30 cases)	23	(77)	6	(20)	1	(3)
Partial (72 cases)	49	(68)	21	(29)	2	(3)
Immobilized (23 cases)	14	(61)	7	(30)	2	(9)

'Aspirin &c' = The common antipyretic tablets kept in the home.

or more limbs had consumed even more tablets. Two men, immobilized by paralysis, admitted to having taken considerable quantities of aspirin in an attempt to keep about. This, I believe, is the danger. Any drug which allows a patient to increase his activity by suppressing the symptoms of pre-paralytic poliovirus infection is a potential danger to him, unless he remains in bed.

Adenovirus infection: On September 16 1959 I attended a schoolgirl of 11 with fever, headache, tender cervical adenitis and an increasingly stuffy nose. In spite of penicillin, oxytetracycline and finally antihistamines, her fever and nasal obstruction continued for six days, after which her temperature dropped, her nose cleared and began to run, in fact 'her cold came out' and she recovered rapidly. Her illness was due to infection by adenovirus type 3 and during the year I attended a total of 44 children with similar symptoms. The characteristic fever does not reach its peak in the first twenty-four hours. Children do not look or feel as ill as the thermometer would suggest; appetites are good; convalescence is immediate and rapid.

Coxsackie type B virus: Coxsackie B infections are frequently encountered; during the year types 2, 3, 4, and 5 have been identified. The majority could be labelled 'P.U.O. with headache', or even 'aseptic meningitis', but this is a severe-sounding name for a relatively mild illness; some have been in fever-free adults or teenagers with sudden thoraco-abdominal pain, in fact mild cases of Bornholm disease. A man of 25, infected with type B2 virus, had an afebrile pleurodynia followed a week later by a painless high fever with headache – Bornholm disease followed by aseptic meningitis. An 8-weeks old baby developed a temperature of 103°F one evening, which returned to normal next morning. Type B3 virus in its stool suggested that the mother's so-called 'rheumatic chest' of the week before had in fact been Bornholm disease.

'WP/60': Turning now to respiratory infections, a striking outbreak of 25 or more cases occurred in February and March, of a clinical syndrome I had not previously encountered. After an incubation period of two days, a young child, seldom over 5, would take ill suddenly with hyperpyrexia and a dry irritating cough; it might be delirious the first night, coughing incessantly, and by the next day have developed massive crepitations in one or both lungs. In several children fever was biphasic, like that of influenza and, in spite of tetracycline, might last from two to six days, sometimes with marked tachycardia (160–180 beats per minute). A full description of the syndrome has been published under the name of WP/60 (Report, 1960*a* and *b*) and I would be interested to hear from anyone who encounters similar cases, since no recognizable infective agent has been identified.

Virus pneumonia: Fig 4 shows how the temperature and other features of WP/60 differed from so-called 'atypical primary virus pneumonia', with its rising titre of agglutinins against streptococcus MG (Wood 1956). In three family outbreaks of this disease, the serial interval was commonly two weeks or more.

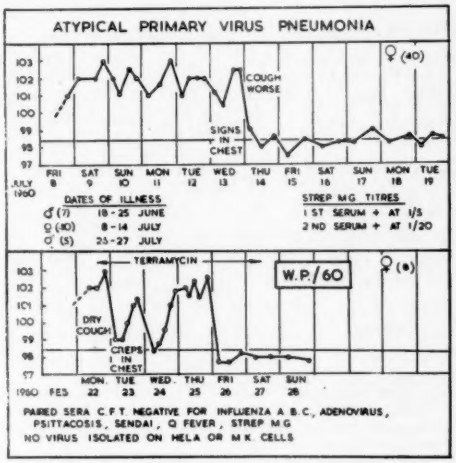

Fig 4 *Two non-bacterial pulmonary infections*

Table 4
Atypical primary virus pneumonia
Serial Intervals in 3 Families

Interval in days	14	15	17	18	20	31
No.	4	1	1	4	1	1

The clinical syndrome is indeterminate until, after several days of headache and fever, local signs develop in the chest, the cough increases and then massive crepitations can be heard – often in the right middle lobe. The disease is highly infectious, even in convalescence. In one group of families this year it passed through six generations of infection in 13 people between June 28 and October 1. Only 2 adults out of 15 close contacts escaped.

Conclusion: Finally, in our preoccupation with exciting new 'seeds', let us not forget the human

'soil' which tolerates so many infectious insults. Among the victims of that adenovirus outbreak mentioned above was a boy of 7, whose gastro-intestinal tract must have been a pathogen's paradise. During the year he suffered from *Salmonella typhimurium*, harboured *Shigella sonnei*, was infected by adenovirus type 3, revealed a silent midwinter sanctuary of poliovirus type 1 and shared a family attack of type 12 streptococcal tonsillitis. At the other end of the scale is a family with 5 children. Last summer I was called to the eldest boy, aged 9, who had a sudden headache and temperature. Almost apologetically the mother asked if I had any special instructions before leaving: 'Remember, doctor, I have never had any of my children feverish and in bed before.'

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Despite the fall in the incidence and mortality of infectious diseases they still cause much disability and involve the general practitioner in much work. Although the virtual defeat of tuberculosis is in sight, more hospital beds in this country are still filled by patients suffering from tuberculosis than by all other infectious diseases put together.[1] Measles in epidemic years provides 300 times as many cases as poliomyelitis, with about 100 deaths, almost as many as occur from poliomyelitis (in 1959 the number of deaths from measles was actually greater than that from poliomyelitis).

In some children measles could still be a serious disease because of its complications, such as bronchopneumonia, otitis media or ophthalmia. Recently, measles encephalitis has come into prominence, and it has been suggested that encephalitis is much more common in the childhood infectious diseases than is evident from clinical observation (Gibbs *et al.* 1959). It has even been suggested that epilepsy and other neurological or psychiatric disorders may stem from a sub-clinical encephalitis complicating an infectious disease (Olivarius *et al.* 1959). Encephalitis and neurological disorders have also followed Asian influenza in which encephalitis has been a complication (Fluett & Hoult 1958).

Better nutrition and living conditions have had a profound effect on the decline of the mortality from measles, and gamma globulin has helped to prevent or to attenuate the attack in day nurseries. A more helpful approach was by vaccination (Enders *et al.* 1959, Schwartz *et al.* 1960), but the vaccine used in the measles epidemic in Panama in the spring of 1959 produced a fever and rash in many of the subjects, although it appeared to protect against measles (Hoekenga *et al.* 1960). A less virulent type of vaccine was required.

There has been a decline in the incidence of whooping cough, and recently a new method of diagnosis has been discovered which claims to be reliable and rapid, giving a result within an hour (Donaldson & Whitaker 1960). If it was possible to diagnose whooping cough promptly we should be able to test various drugs in the early stages to see if they were effective in stopping the advance of the disease. At present immunization was still our main defence against whooping cough.

Scarlet fever still produces about 30,000 cases a year, and although it is now not a serious disease, hæmorrhagic nephritis has been found to follow in some who have been infected by type 12 strain of Griffith streptococci (George *et al.* 1958, Pleydell & Hall-Turner 1958). Overcrowding in classrooms is a factor in the spread of scarlet fever (Ministry of Health Report 1956).

Many doctors have never seen a case of diphtheria so that some cases might go unrecognized. The delay in the diagnosis might be dangerous both to the patient and to his contacts as well. There has been a fall in the number of immuniza-

[1] *Med. Offr.* (1960) **104**, 96

tions in the past few years, partly due to time spent in vaccination against poliomyelitis, also because of the risk of provoking this disease.

Dysentery was on the increase and though generally a mild disease could be serious to very young children and particularly dangerous if it broke out in a maternity home or an institution for old people. The main method of spread has been through lavatory seats, plug handles, door knobs, etc. (Hutchinson 1956) and improvements in hygiene, particularly in schools, could help to eliminate the disease. Among the normal population the number of symptomless excreters varies from 0·3 to 3 per cent, but they would not appear to be important in the outbreak (Leff 1954, Ross 1957). It was doubtful whether the exclusion of carriers from schools or day nurseries helped to limit the extent of the outbreak.

It has been estimated that there are at least 50,000 cases of *Salmonella typhimurium* food poisoning per annum in England and Wales, and it has been suggested that general practitioners are not enthusiastic about these cases and therefore do not bother to report them. This is a pity since individual cases can now be identified with great precision and better notification could help in controlling infection. For example, in 1958 the isolation of a 20A phage type solved the problem of a widespread outbreak – 471 cases scattered through a population of 17 million in the home counties were traced to a cattle distribution centre near Oxford. The importance of Salmonella carriers has declined during the last ten years although the rate is estimated to be 2·5 carriers per thousand population (Public Health Laboratory Report 1959*a*). Salmonella is widespread among many foodstuffs. For example, it has been found in 10% of boneless meat and 4% of carcase meat (Hobbs & Wilson 1959), and also in animal feeding stuffs (Public Health Laboratory Report, 1959*b*) and in coconut (Galbraith *et al.* 1960).

Staphylococcal infection in food poisoning is common and can be identified by the bacterial phage pattern. Nose, throat, hands, and lesions such as boils, carbuncles and whitlows are the main reservoirs of staphylococcal infection. Investigations of outbreaks therefore include the isolation of coagulase-positive staphylococci not only from food but also from the known source of infection. The manufactured semi-preserved foods eaten cold – for example, hams, pressed meats, brawns and pies – are most commonly involved because hands contaminated by secretions from nose, throat and other lesions transfer the infection to the foods they touch.

Although they inhibit the growth of many organisms, the salts used to preserve some meat stuffs are ineffective against staphylococci. The organism also grows readily in the cow, and can easily contaminate milk and other dairy products. Enterotoxin in spray dried milk has sometimes given rise to food poisoning both in Britain and the United States.

A third organism commonly responsible for cases of food poisoning is *Clostridium welchii*, which is widely distributed in the environment (Hobbs & Wilson 1959). Its spores are particularly hardy and the only effective method of control lies in regulating cooking and storing of meat dishes. The time between cooking and eating should never exceed one hour unless there is a storage at about 60°C or in the cold; it is necessary to cool meat rapidly, remove danger spots such as chopping boards and avoid cross contamination in the kitchen (Bloss 1959).

There is no doubt that the general practitioner can play a large part in discovering and notifying cases of food poisoning and also in their investigation. As a part-time factory doctor and a frequent visitor in the home, he can help to improve standards of food hygiene.

The only safe way of preventing food poisoning is the destruction of bacteria in food stuffs immediately before their delivery to consumers in the same way, for example, as drinking water. The other paramount matters are adequate cooking and refrigeration.

Between 1950 and 1957 more cases of poliomyelitis were diagnosed in men than in women – except in the 15-24 age group. On the other hand 5% more women were paralysed. Infants showed the highest proportion of paralysed cases but the largest reduction in the death-rate. The least fall in mortality was in the age group 25 and over (Martin 1959).

There were still differences of opinion on the best type of vaccine to be used. The basis upon which the U.S.A. Public Health Department has approved the Sabin as against the Koprowski vaccine has been challenged (Koprowski 1960).

The new viruses were very puzzling in their effects. Many patients originally diagnosed as suffering from non-paralytic poliomyelitis had turned out to be cases of aseptic meningitis. Many viruses could produce this illness and they included mumps, lymphocytic choriomeningitis, Coxsackie, and the ECHO viruses. The ECHO and Coxsackie viruses might produce paralysis as well (Steigman 1958). The Coxsackie virus, widely prevalent in 1958, had been isolated from cases of non-paralytic poliomyelitis, aseptic meningitis and Bornholm disease, from the throats of patients suffering from upper respiratory tract infection and from the fæces of normal children (Cook 1959). Today, as many as 19 different antigenic types of Coxsackie had been discovered, together with 29 ECHO viruses (Rhodes 1960).

It has been estimated that 30% of general

practice is virus respiratory diseases resulting in an enormous economic loss.[1] Influenza covers many acute febrile respiratory diseases which may have a varying ætiology. A group of viruses (hæmadsorption) have produced respiratory infections ranging from minor forms of illness resembling the common cold to severe illnesses of bronchitis, bronchopneumonia, croup or severe pharyngitis (Parrott *et al.* 1959). A severe form of bronchiolitis in infants under the age of 18 months, associated with familial respiratory infection has now been recognized,[2] and in a recent outbreak 11% showed evidence of adenovirus infection but no cause or relationship was established (Sandiford 1960). Adenovirus affected both children and adults, giving rise to disorders such as pharyngitis, conjunctivitis, acute febrile diseases, tracheobronchitis, bronchiolotis and atypical pneumonia. Gastro-intestinal symptoms and meningism have also been found, especially among children. These viruses may be spread not only through the air but also through the gastro-intestinal tract and are particularly likely to cause outbreaks where there is close contact, such as in barracks and schools (WHO 1959).

Better living conditions and better standards of hygiene undoubtedly play a large part in eliminating infectious diseases. Much help, however, can be given by methods of vaccination and immunization, early diagnosis, isolation and treatment. We can look ahead in the future confidently for the complete elimination of infectious diseases (Zhdanov 1959).

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Virus infection occurs in three modes – that in association with clinically manifest disease, that occurring in a subclinical manner, and the state of persistent latent infection which is also clinically inapparent. Clinicians only recognize the first of these three modes but the others are equally important. Mere recovery of a virus from human secretions, tissues or excreta at a time of illness is therefore inadequate evidence of a causal relation between the virus and the illness. Koch's postulates modified for viruses must be applied and wherever appropriate the reproduction of clinical illness by the inoculation of virus cultures into volunteers may supply the crucial evidence of relationships. All these considerations apply with particular force today when the virologist has enormously better facilities than in the past for recovering viruses by tissue cultures using the basic techniques evolved by Enders and his colleagues (Weller *et al.* 1949). In fact, with many of the newly-found viruses of the alimentary and respiratory tracts, virus isolation is the best method of diagnosis. This is because serological evidence of a rise of antibodies which has been so useful in the case of influenza, is rendered difficult in other infections by the multiplicity of viral antigenic types. Common complement-fixing antigens exist only in the case of the adenoviruses. Many types of the Coxsackie and ECHO viruses are known and no common antigen has yet been discovered. Having cultured a virus from human specimens, it is still necessary however, to perform serological tests with acute and convalescent serum specimens. The techniques available for these differ but they include neutralization tests in tissue culture.

Relationships between Certain Syndromes and Viruses

(*a*) *Exanthemata:* Small-pox is usefully investigated using material from crusts and this may be very important when dealing with modified disease in previously vaccinated persons. Measles virus though more difficult to work with is interesting particularly because of the possible antigenic relation to dog distemper virus. The evidence for the latter is conflicting but it would, if true, suggest the type of resemblance known to exist between other human and animal viruses. A living attenuated measles vaccine has been developed by Enders and others (1959). It produces immunity against the natural disease at the

expense of a modified illness similar to measles when modified by prophylactic gamma globulin. Trials in children have been reported from the U.S.A. (Katz *et al.* 1960). Protection against measles is desirable if only because of the respiratory and occasional neurological complications.

Roseola infantum shown by Neva (1956) to be due to enteroviruses now occurs in epidemic form associated with aseptic meningitis. ECHO 9 virus was the cause of the syndrome in 1956 and again recently in 1960. A few other types of ECHO viruses produce rashes but the more usual clinical manifestation is aseptic meningitis – a syndrome due to many different viruses including poliovirus and certain Coxsackie viruses.

(*b*) *Respiratory syndromes:* Much confusion still exists because of the clinical difficulty in differentiating the various forms of acute respiratory disease and the large number of different respiratory tract viruses now known. The febrile catarrh of servicemen described in 1938 is known to be chiefly due to adenoviruses but the Coe virus (Lennette *et al.* 1958) and possibly other agents may at times be concerned. Latent infection with certain types of adenoviruses is common in childhood. Atypical pneumonia is now known to be due to the agent of Eaton and others (1944) which can be cultivated in the fertile hen's egg and studied by fluorescent microscopy. That form of atypical pneumonia unassociated with the development of cold red cell agglutination may however be due to adeno- or other viruses. Croup in childhood appears often to be due to a new group of hæmagglutinating viruses which grow in monkey kidney tissue cultures and are now termed the para-influenza viruses. They seem less important as a cause of disease in adults. The most interesting recent discovery is that of the technique of Tyrrell & Parsons (1960) for cultivating the common cold virus in human or monkey kidney tissue culture. The virus will grow and produce cytopathic effects at 33°C but not at 37°C and special media are needed. Several such cold viruses have also been recovered from natural colds in Sheffield (Hobson & Schild 1960). The long-awaited ability to grow this virus will stimulate a new effort into the correlation between clinical illnesses involving the respiratory tract and the viruses which can cause them

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Section of Obstetrics and Gynæcology

President W R Winterton FRCOG

Meeting October 28 1960

President's Address

The Story of the London Gynæcological Hospitals

by W R Winterton FRCOG (*London*)

After the dissolution of the monasteries by Henry VIII in the sixteenth century, St Bartholomew's and St Thomas's were in effect the only two general hospitals in London for the next two hundred years. While the population was living in small scattered villages the need for hospitals was not very obvious. But with the eighteenth century came the Industrial Revolution and the growth of the big towns, so that more sick people were seen in small areas and something had to be done to help them. It was the beginning of England's social conscience, an increased consideration for one's neighbour, the time of Wesley and the evangelical movements.

Most of the London Teaching Hospitals were founded in the middle of the eighteenth century by charitably minded laymen. About this time also the lying-in hospitals were founded. The General Hospitals excluded 'incurables, lunatics, V.D. and smallpox'. They also largely excluded malignant diseases and gynæcological cases because these were mainly long-stay patients for whom little could be done, and the waiting lists were so long that with the very limited number of beds it was not considered justifiable to admit them.

During the nineteenth century we see the beginning of the rise of the specialist and the special hospitals. Since so many conditions were refused admission to the general hospitals there was little advance in knowledge in the special subjects. Also the more charitable outlook of the times considered that it was a disgrace that such patients were not receiving the medical attention to which as human beings they were entitled. While many of the general hospitals were founded by laymen out of pity for the sick poor, it is most noticeable that nearly all the specialist hospitals were founded by medical men who were anxious to advance their knowledge of a particular specialty.

The specialist hospitals (Table 1) multiplied rapidly. The earlier ones were eye hospitals founded in response to the great need for the care of soldiers returning from the Napoleonic wars.

Table 1
Special hospitals (other than mental hospitals) founded during the nineteenth century

	United Kingdom	*Scotland*
1800–09	4	1
1810–19	11	–
1820–29	9	1
1830–39	9	2
1840–49	12	–
1850–59	23	1
1860–69	32	2
1870–79	30	3
1880–89	29	6
1890–99	10	1
	169	17

Foundation of The Hospital for Women

On September 1, 1842, Dr Protheroe Smith called together a provisional committee with the object of founding a Hospital for Diseases of Women. He was then aged 33 and was Assistant Lecturer in Diseases of Women at St Bartholomew's Hospital. For five years prior to this, that is from the age of 28, he had been trying to found the hospital but had met with great opposition. Finally he succeeded in interesting a number of men of influence who formed this committee. He wrote deploring the want of suitable accommodation for treating patients labouring under the diseases peculiar to females, and proposing that a Hospital for Diseases of Women should be founded. He pointed out the limited means at the time for obtaining professional information on this interesting department. He had worked for some years with Dr Edward Rigby, Examiner in Midwifery to the University of London and Lecturer on Midwifery and Diseases of Women at St Bartholomew's, and had collected a considerable volume of information, but opportunities had been much curtailed by lack of hospital accom-

modation. He asked whether as alternatives it would be better to appropriate a few wards in the large hospitals which already existed, or whether the suffering poor could be attended in their homes.

At that time there were only two hospitals in the whole of the British Isles which had set apart a ward for these cases – Dublin and Guy's. The rest were unable to spare the beds. I quote from his letter:

'In consequence of the delicacy of treatment to which the women of this country have always been accustomed it is quite impracticable without outraging English modesty for the physician or surgeon to give requisite attention to such cases as may promiscuously occur in the general hospitals where he is usually accompanied in his rounds by a large number of pupils.'

In this appeal he was supported by letters from the leading specialists of the time.

Dr Samuel Merriman of the Middlesex Hospital (Fig 1) stated that though uterine disease was very common among outpatients he was only able to have one patient in hospital at a time.

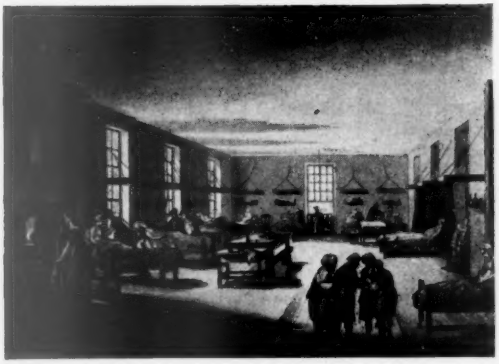

Fig 1 *A ward of The Middlesex Hospital. From a painting by Thomas Rowlandson*

Dr Rigby agreed with the need for such a hospital and stated that there was no class of disease including infectious diseases and phthisis which was admitted so unwillingly into our great hospitals as this. It was a class of disease which was little understood, and the treatment was difficult but none was more completely neglected by every branch of the profession. It required different attendants to the ordinary nurses and therefore would be better in special wards, but he had been unable to obtain one when he was at St Thomas's or later at St Bartholomew's, and he therefore agreed that a special institution was required.

Dr Ashwell of Guy's stated that the Treasurer, Mr Harrison, had recently set aside Petersham Ward for these cases with tremendous benefit, but more was required. The great Dr Richard Bright of Guy's reinforced Dr Ashwell's letter. Dr Kennedy Master of The Lying-in Hospital, Dublin, wrote that he had started a special ward which was invaluable.

James Young Simpson referred to the immensity of good resulting from the provision of a special ward in Dublin. Edinburgh lacked not the will but the means. General surgeons and physicians were ignorant of these conditions, neglected them, and refused their admission to their wards.

Dr Warrington of Philadelphia wrote a charming letter similar to the others, and ended by saying 'May the British add this to the number of her noble charities and may we her children speedily imitate her good example'.

I have given these letters at some length – and I would quote more but they are largely repetition – in order to give some sort of picture of the conditions of 1840, only a hundred and twenty years ago: the confessed ignorance, the terrible lack of opportunities to learn more and to teach our specialty.

Fig 2 *The Hospital for Diseases of Women, Red Lion Square*

On April 13, 1843, under the Presidency of the Duke of Rutland, the Hospital was founded. Its original title was The Hospital for Diseases of Women. A house was taken in Red Lion Square from midsummer 1843 (Fig 2). A matron and servants were engaged, the total for salary and

wages amounted to £56 15s 0d (there was no mention of nurses). The cost of running the hospital was expected to be £600 per annum.

On January 25, 1844, the first hospital in the world for Diseases of Women received its first patients. There were only 11 beds in two wards. During that year there were 28 inpatients and 73 outpatients.

The founder, Protheroe Smith (Fig 3), was born in 1809. He was an earnest and religious young man from a large family in Bideford, son of a doctor, and originally intended to go into the Army. A commission had been promised him, but he injured his hip in some athletic sport. He therefore decided to take up medicine and become a military surgeon, but he soon became interested in the science of medicine and gave up any idea of a military career. In 1833 he qualified MRCS from St Bartholomew's where he had obtained first prize in Anatomy, Physiology and Surgery, and was appointed Assistant Lecturer in Midwifery and Diseases of Women. His duties involved seeing outpatients, 100–150 a week. In 1842 he performed an ovariotomy, without an anæsthetic of course, on a patient who was alive forty-five years later (*Lancet* 1889). This was the second ovariotomy known in London but does not seem to appear in the official records of the operation, though Sir Spencer Wells mentions it vaguely in his book (Wells 1885). The only earlier ovariotomy in London was by Morgan, Key and Bransby Cooper of Guy's who were general surgeons (Spencer 1934). Protheroe Smith is also reported to be the first in London to use an anæsthetic in labour and he wrote articles giving the Scriptural support for such anæsthetics.

He took the MD Aberdeen in 1846 and the MRCP in 1847. From what I have read about him he appears to have been a good operator, and a great inventor of surgical gadgets and instruments which he described in the medical journals, but he did not write much apart from this. He retired in 1885 from the active staff of the Hospital for Women and died in 1889.

The foundation of this the first hospital devoted entirely to diseases peculiar to women is a great milestone in British medicine and gynæcology and has hardly received the recognition it deserves; still less has the pioneer position of Protheroe Smith.

The difficulty of collecting funds was enormous. The name, The Hospital for Diseases of Women, to Victorian England suggested VD for which few were prepared to subscribe. Consequently in 1845 the name was changed to The Hospital for Women, a name to which it is proudly entitled as being the first in the world.

It is difficult for us to picture to-day a gynæcological hospital in which the average stay of the patients was eleven weeks. The annual report refers to operations performed but gives no details of their nature and no notes survive. It must be remembered these were pre-anæsthetic days, and pre-antiseptic days.

By 1849 the number of outpatients had increased to 5,000. This concentration of gynæcological cases could be studied and something could be learned. With only two outpatient days a week, an average of 50 patients a session would hardly seem ideal for careful study, which was one of the objects of the foundation, but it did provide enormous experience. By contrast the long stay of the inpatients gave ample opportunities. This was all done in one house in Red Lion Square.

Fig 3 *Protheroe Smith*

Fig 4 *A ward in The Hospital for Ladies. From a painting by Winterhalter*

Gynæcological Wards in General Hospitals

By 1851 the hospital had outgrown its accommodation and moved to its present site in Soho

Square and the number of beds was increased to 20. At this time it was stated in the annual report that as a result of the example of the Hospital for Women many general hospitals had opened gynæcological wards. Where these were I do not know. Mr T E Cowan, the Records Officer at The Middlesex Hospital, kindly wrote to the other teaching hospitals and Table 2 is the answer. However, I think we can take it that between 1842 and 1850 gynæcological cases were admitted and perhaps were all accommodated together in part of a ward. This at least was a great advance.

The Annual Reports for these years record the visits of a large number of foreign surgeons and physicians. Travel could not have been easy and it says much for the interest that this special hospital was arousing that they should have considered it worth their while.

Table 2
Dates of first opening of gynæcological wards

1831	Guy's Hospital
1846	University College Hospital
1861	St Bartholomew's Hospital
1862	Charing Cross Hospital
1873	St George's Hospital
1876	The London Hospital
1882	Royal Free Hospital
1885	The Middlesex Hospital
1886	St Mary's Hospital
1888	St Thomas's Hospital
1915	Kings College Hospital
1924	Westminster Hospital

A year or two later there is another note of visits from other centres with a view to establishing hospitals, in Leeds, in Boston and in another city in America. Presumably this refers to the Marion Sims Hospital which was founded in New York in 1852.

The Samaritan Hospital

The Samaritan was founded in 1847 by Dr William Jones, aged 36, though Dr Henry Savage is often given the credit. It was first called the Gynepathic Institute Free Hospital and began as a rather less specialized hospital – with 8 beds for women and children. For the first three years men were treated as well, but only as outpatients. In 1854 Spencer Wells was elected to the staff of the Samaritan where he carried out his famous series of ovariotomies which caused such a furore throughout the country.

The abdomen was becoming for the first time a hunting ground for the surgeon, but carried the penalty of what to-day would be considered a prohibitive mortality. It was not a time for the squeamish, and it is possibly the ruthlessness and individuality of many of our predecessors that enabled them to advance at this time when new surgical techniques were emerging, and in particular during that dangerous gap between the introduction of anæsthetics and before the introduction of antisepsis.

There was growing opposition in the medical world to the existence of the special hospitals and on July 16, 1853, the following paragraph appeared in the *Lancet:*

'*Unprofessional Advertisements.*—Our attention has for several weeks past been attracted by the frequency of appeals made for pecuniary aid to certain medical institutions by public and oft-repeated advertisements in the leading newspapers. Such constant demands for institutions appropriated to special diseases (that for example, in Soho Square) savour more of legitimate quackery than of philanthropy. The introduction of the name of a leading and highly accomplished physician, who it is well known withdrew his support from the institution alluded to some years ago, and after conviction that he could not sanction many of the proceedings that took place, is a liberty which no medical man, except those belonging to the quack's class, would venture to take' (*Lancet* 1853).

The opposition to the special hospitals probably reached its height in 1860 and 1861. At the BMA meetings both at Torquay and Canterbury there were special sessions set aside to discuss the problem. During those years there were no less than seven editorials on the subject in the *British Medical Journal* (1860, 1861) in every case condemning the rise of the special hospitals in robust Victorian language. The arguments against the hospitals were as follows: (1) That they were robbing the teaching hospitals of all their teaching material. (2) That they 'were all founded in the grossest self seeking on the part of some individual and they are matured only through mendicancy'. (3) That they were uneconomic and cost nearly double as much per patient to run owing to their small size. (4) That they saw patients who could afford to be treated in their homes. (5) That they did nothing to advance medicine and that 'splitting up into Specialties destroys that unity of disease which the philosophic mind should always keep in view.' (*Brit. med. J.* 1860, 1861).

It was pointed out that perhaps there would be advantages if the general hospitals put aside special wards for some of the major specialties and that three of them had already set aside wards for diseases of women, but the editorials went on to say that there were dangers even in that and it might prove a mistake. The writers of the editorials found it even more infuriating that the public in their ignorance had a misplaced faith in specialists and special hospitals and flocked to them in their thousands from all parts of the country. It is obvious that in these circumstances members of the staff of the general and the special hospitals formed two separate camps, and it was not till about 1880 that individuals were on

the staff of both special and general hospitals.

By 1860 The Hospital for Women had increased to 25 beds but the average stay was still nine weeks. The number of outpatient attendances was 12,000 and they were charged one penny each. The outpatient department was still open on two days a week only. It was then decided to appoint two assistant physicians, the appointment being for one year only. This interesting innovation was made purely with the idea of training and corresponds to the later clinical assistants. The full staff consisted of only 2 physicians and a surgeon. The difference between a physician and a surgeon was one of qualifications. The work seems to have been the same. Protheroe Smith was appointed at the foundation as a surgeon, his only qualification being MRCS, but when he took his MD two years later he was promoted to being a physician. Sanderson, who was appointed as a surgeon, took his MD and resigned in consequence to be appointed as a physician two years later. At the Samaritan, on the other hand, Spencer Wells kept the surgery largely in his own hands.

In 1862 the number of beds at The Hospital for Women was increased from 25 to 50 and the first house surgeon was appointed.

In 1869 the first Pay Block in the British Isles for those of limited means was opened by the Princess Mary Adelaide. The demand for the pathetically few free beds was immense and there were many, such as wives of small tradesmen, governesses (a large class in those days), wives, widows and daughters of professional men and so on, who could afford to pay for their medical care but who were not in a position to be looked after at home. There was an extremely good leader in *The Times* headed 'The Hospital for Ladies' (*The Times* 1865). This pointed out that when the lady of the house was ill she was well cared for and waited on by servants. If a governess or a poor relation became ill, the servants would not wait on her adequately. This paying wing would keep these patients from competing with the so-called 'indigent poor'.

The rooms (Fig 4) varied in size from 1–5 beds with curtains round each, and the cost from $1-3\frac{1}{2}$ guineas a week inclusive. There were 23 beds. It even included what is considered a modern addition in many hospitals to-day 'a drawing room' for convalescent patients. There was also a lift, which is specially noted in the newspaper reports of the opening ceremony as it was a rarity in hospitals at this time.

Unfortunately we have only one volume of patients' notes of the first forty years, that for 1870. We know operations were done from the first opening of the Hospital but the overall mortality remained in the neighbourhood of 1–2% till 1867 when it rose to 4·5% of all admissions, and in 1873 was 10% of which 19 out of the 32 deaths were from post-operative peritonitis. I think we must assume from this that the number of operations had greatly increased. In 1869 there were 238 admissions and 39 operations performed with an overall mortality of 4·4%. This is an operation rate of 16% and an operative mortality of 25%. No operation was allowed by the rules without prior consultation between two members of the staff. Until shortly before this time no cases of malignant disease were admitted but now patients with early carcinoma of the cervix were allowed in hospital.

Sir Spencer Wells (Fig 5) of the Samaritan was the great figure in the gynæcological surgical world, though to judge from the history of the Samaritan Hospital, he was not a very easy colleague and did little to encourage others. Between 1856 and 1867 he performed 100 operations of ovariotomy. When he retired from the active staff of the Samaritan in 1877 the results shown in Table 3 were published:

Table 3
Result of ovariotomy 1877

	Cases	*Recoveries*	*Deaths*	*Mortality %*
Three large hospitals	61	24	37	60·65
Guy's Hospital	82	39	43	52·43
Hospital for Women	71	44	27	38·16
Samaritan Hospital	281	214	67	23·84

The lower mortality rate is a very striking tribute to the special hospitals.

Spencer Wells was born in 1818, lived at Golders Hill, was PRCS in 1882 and died in 1897. The Samaritan was his only hospital apart from two years at St Peter's.

In 1870 lectures were given in the winter evenings by the staff of The Hospital for Women to medical practitioners. These were so well attended that they were repeated every year for many years. I do not know very much about the set teaching of postgraduates, but as far as I know these are the first in gynæcology. Incidentally, the hospital report for that year refers to the 'modern name of gynæcology'. The dictionary states that the first record of the word was in the eighteenth century but it was not in common use till the late nineteenth century.

In 1870 funds were so low that half the beds had to be closed. It was then decided that with the very long waiting list they would open some of the beds for patients who could pay 10s 6d a week, the cost of their food and washing. This was a great success and these beds were kept continually full. There were therefore three categories of patients in the hospital – full paying patients, contributory patients and free patients, similar to the situation to-day.

Chelsea Hospital for Women and the Grosvenor Hospital

In 1871 the Chelsea Hospital for Women (Fig 6) was founded by Dr James Aveling 'for the reception of Gentlewomen of limited means and women of respectability suffering from curable medical and surgical diseases'. Like The Hospital for Women and the Samaritan it began with 10 beds. It opened in King's Road where it remained til 1883 when it moved to Fulham Road with 63 beds.

Dr Aveling was born in 1828 and qualified from Aberdeen. He had an unusual career. He was a

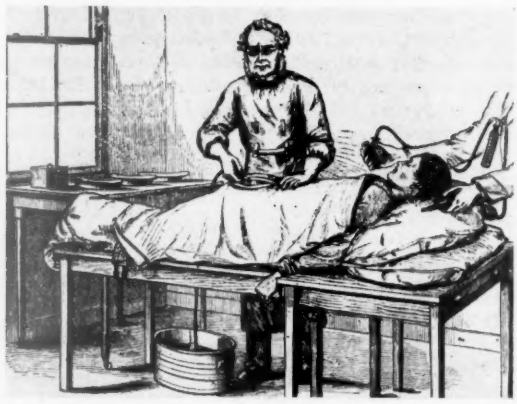

Fig 5 *Sir Spencer Wells*

general practitioner in Sheffield and in 1865 founded the Sheffield Hospital for Women, now the Jessop Hospital. Three years later he moved to London where he founded the Chelsea Hospital for Women. He was on the staff until his death from typhoid in 1892. He is best remembered for the Aveling repositor for inversion of the uterus. His obituary states that having come from a mechanically minded family he invented many surgical gadgets, and his brother invented the steam roller (*Lancet* 1892). The firm Aveling Barford is still well known.

The Grosvenor Hospital in Vincent Square was opened in 1865. The Grosvenor and the Samaritan were for women and children. Both these hospitals were special only in the sense of limitation of sex, though naturally there was a preponderance of gynæcological cases.

What treatment was carried out at the special hospitals during these first forty years – years which were perhaps the most momentous in the evolution of surgery, in that they witnessed the introduction of anæsthetics, the work of Pasteur leading to the introduction by Lister of antiseptic surgery?

Ovariotomy we have already discussed. It was to all intents and purposes the only gynæcological abdominal operation which was done, and even this carried a high mortality. A few hysterectomies were attempted but were almost invariably fatal. Operations were done for perineal tears, and vesico-vaginal fistulæ, at that time a commoner complication of obstetrics than in this country to-day. Pelvic abscesses seem to have drained themselves spontaneously through the rectum. Fibroids and menorrhagia were treated by injecting fused potash into the uterus at frequent intervals. Carcinoma of the cervix was treated by

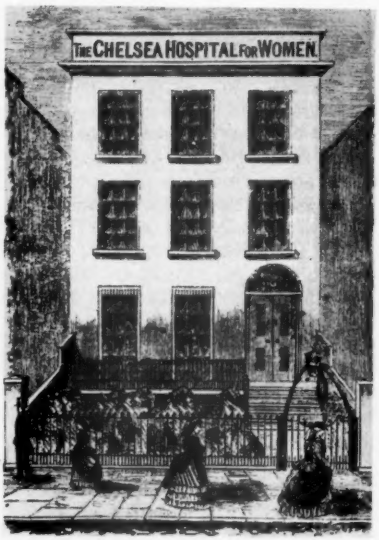

Fig 6 *The Chelsea Hospital for Women, King's Road*

scarification by various cauterizing agents. Leeches were in common use and were fastened on to the cervix for pelvic inflammation. There are several records of patients refusing this treatment.

A large proportion of the patients were suffering from misplacement of the uterus. They stayed in hospital for many weeks having their uterus pushed forwards either digitally or by means of uterine sounds, and retained in position by pessaries of many shapes and designs. This was done in the wards once or twice a week, and immense importance was attached to the position of the uterus. The first case admitted to the Chelsea Hospital for Women was one of paralysis. I quote from the first Annual Report:

> 'Seven years before admission she had a severe fall injuring the lower part of her spine and displacing her womb to such a degree as to induce progressive

paralysis of the left side to an extent which prevented her from following her ordinary avocation. She remained in hospital thirteen weeks, when she was discharged cured and now holds a responsible situation in Surrey.'

Those who have read Sir Spencer Wells' book on Abdominal Tumours, written in 1885, know what a very dangerous operation hysterectomy was, even done by that master of technique and courage. Bland-Sutton, working at the Chelsea Hospital for Women from 1895 to 1910, worked out the technique and made it a comparatively safe operation.

Bland-Sutton (Fig 7) is one of the most illustrious names in surgery. He qualified in 1882 and was appointed to the staff of The Middlesex Hospital in 1886 only four years after qualifying. He never held a house appointment. As a member

Fig 7 *Sir John Bland-Sutton Bart*
'Some surgeons cut you up like mutton,
But that is not the way with Sutton;
Bland as his name, though stern of eye,
He couldn't bear to hurt a fly.'
Ind' et fecit George Belcher
Reproduced by kind permission of Punch

of the Junior Staff he had no beds under his care but took over those of his Seniors during the summer holidays. His spare time was spent at the Zoo doing post-mortems on animals, studying comparative anatomy and pathology. It was as a result of his work there that he devised the technique for hysterectomy.

In 1895 Bland-Sutton was appointed to the staff of Chelsea Hospital where he remained for fifteen years and his work there did much to raise the status of gynæcology. In 1910 he was elected to the Council of the Royal College of Surgeons and resigned from Chelsea. He became President of the Royal College of Surgeons in 1922. Bland-Sutton was an example of the bed starvation from which junior staff of the general hospitals suffered and it is the beds to which Bland-Sutton had access at the Chelsea Hospital for Women that gave him opportunities to make his enormous contributions to the advance of gynæcological surgery.

About 1880, each of the hospitals appointed a pathologist. This shows the changing outlook to disease. Henceforth pathology was to be added to the rather more mechanical approach to disease of earlier times. John Bland-Sutton and also Victor Bonney, whose work covered the years 1900–1940, would wish to be remembered as much for their pathological contributions as for their operative skill. In 1880 at The Hospital for Women 139 operations were performed with 30 deaths, a mortality of 21%; in 1920, 1,000 operations were carried out with 14 deaths, a mortality of 1·4%.

With a slow turnover of inpatients a considerable concentration of patients with similar complaints is necessary for any advance in knowledge to take place. Only by these means can the pathologist carry out research and the clinician accumulate experience, and it is only by constant operating that surgical technique can be perfected. The special hospitals were becoming accepted by the general hospitals and at last members of their staff were also working at the special hospitals. The number of beds in the teaching hospitals allocated to the gynæcological departments, in particular to the junior members, was and still is lamentably small. Victor Bonney had three beds at the Middlesex Hospital until he became Senior at the age of 58 in 1930, and it was at The Chelsea Hospital for Women that he did so much which made his name world famous. If a man intends to take up singing, or playing the piano as a profession, he begins when he is young and practises for several hours every day. On the other hand if he intended to do surgery, fifty years ago he began to operate when he got on the senior staff of a hospital when he was middle aged, and even then he only had sufficient beds to do an occasional operation. It was here that the special hospitals did so much to bring about the high standard of operating that was and is seen in this country. Finally, of course, there is the exchange of ideas among colleagues who are drawn from many different schools of medicine. At most general hospitals at this time there was only one or at the most two gynæcological surgeons on the staff and often they were not on speaking terms.

National Health Service

In 1948 with the coming of the National Health Service the special hospitals entered a new phase. The Hospital for Women became an annexe of the Middlesex, and the Samaritan of St Mary's, and are now absorbed into undergraduate teaching hospitals, while Chelsea Hospital for Women became part of the Postgraduate Federation and maintained its independence. The first two could at the whim of the Board of Governors be changed to some other branch of medicine or closed down for ever. Such insecurity is bad for the morale of the staff and the establishment of a progressive department. What is the answer? With to-day's costs small semi-independent hospitals are hardly economic, though economics should not be allowed to carry too much weight. The overhead costs of the ancillary departments required for research and treatment have to be spread over a greater number of beds. The recruitment and training of nurses of a high standard is a difficult problem in such hospitals. All must agree that the need for a relative concentration of patients of one specialty for training and research is as great to-day as it was a hundred years ago, but specialization is so great to-day that an isolated unit is in danger of losing touch with the complex advances in general medicine and surgery, and close contact must be kept with medical and surgical colleagues, and this the invigorating atmosphere of a general hospital provides. On the other hand, by spreading gynæcologists thinly over a large number of hospitals we lose touch with our own colleagues and perhaps the stimulation of competition within our own specialty.

I always felt that the ideal was bigger general hospitals which included sufficiently large special departments so that the mother hospital became in effect a collection of special hospitals working together. Such is seen in North America and I have had the privilege of working in one of 1,400 beds. Yet what it gains by having enough gynæcological colleagues and enough gynæcological patients, it loses by its vastness and the fact that the various specialties form their own little groups and tend to cut themselves off from their general colleagues. Perhaps that is because by our standards they are overstaffed. The total consultant staff of our teaching hospitals averages about 50 consultants, whereas there it is nearer 200.

Whatever the future may hold, it will be one of the great tragedies for our specialty if the specialist hospitals disappear from our midst. May they continue either in some modification of their present form, or under the benevolent wing of a general hospital. But come what may, the great missionary work of those young pioneers of a hundred and twenty years ago has brought undreamt results and I hope their contribution will never be forgotten.

Acknowledgments: I should like to acknowledge the help I have received from the Records Officers of all the Teaching Hospitals, to Mr M S Turney at The Middlesex Hospital Photographic Department and to Dr E H Protheroe Smith for photographs and other information about his great-grandfather.

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Section of Experimental Medicine and Therapeutics

President A C Dornhorst MD

Meeting November 8 1960

Discussion on Normal and Abnormal Willed Movement

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Sir Charles Sherrington maintained that all movements were superimposed on a background of muscle tone, the degree and extent of which varied from movement to movement. To-day this view is generally held, and whether one is considering normal or abnormal movements, willed or otherwise, the degree and distribution of the accompanying muscle tone are of singular importance. However, a recurring problem is the nature of muscle tone. Tone has received many definitions, both from clinicians and physiologists, and will be used here to signify the resistance to stretch offered by striated muscle *in situ*. This resistance to stretch is what the clinician attempts to estimate – mentally freed from influences due to joints and ligaments – when he manipulates the limbs of a patient during the course of a neurological examination, and it is with the mechanisms underlying this resistance that this paper will be concerned.

Part of the resistance to stretch offered by striated muscle *in situ* is due to the stretch reflex. From Sherrington's time this reflex has been subdivided into the phasic stretch reflex and the static stretch reflex. The former is the reflex contraction to sudden transient stretch, while the latter is the outcome of prolonged or maintained stretch.

Clinically the sensitivity of the phasic stretch reflex may be estimated by eliciting the tendon-jerk. The reflex pathway involved is illustrated diagrammatically in Fig 1. The afferent neurons are mainly fast-conducting – and therefore large diameter – nerve fibres, arising from the primary annulospiral endings within the muscle spindles. These afferent fibres pass through the grey matter of the spinal cord to end monosynaptically almost exclusively on the large anterior horn cells of the motor neuron pool innervating the muscle from which the afferent fibres originate (Lloyd 1943). For this reason the stretch reflex is more or less

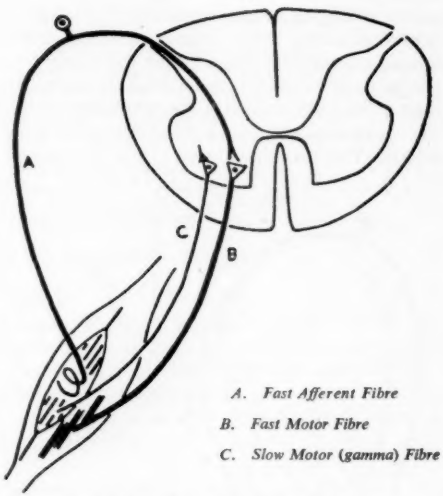

Fig 1 *Spinal pathway of phasic stretch reflex*

strictly confined to the particular muscles stretched. Fig 1 also shows the slow conducting, small diameter motor fibres which arise from small anterior horn cells, and which innervate the specialized intrafusal muscle fibres within the muscle spindles. It is by varying the discharge along these small motor fibres that the degree of shortening of the intrafusal muscle fibres may be altered, and the sensitivity – or bias – of the primary annulospiral endings to superimposed stretch thereby varied. Indeed the gamma system, which includes the small anterior horn cells, their axons and the specialized intrafusal muscle fibres which they supply, provides a means by which the sensitivity of the phasic stretch reflex may be varied. That the gamma system of man is con-

tinuously active during the waking state may be inferred from the experiments of Buller & Dornhorst (1959), while experiments suggesting that the degree of gamma system activity may be increased during reinforcement have been carried out by Somner (1940), Paillard (1955) and Buller & Dornhorst (1957). Benson (1959) has similarly inferred changing gamma bias during labyrinthine reflexes in man. These changes in small anterior horn cell activity are presumably produced by changing patterns of descending extrapyramidal impulses, and it would appear that the supraspinal control of the phasic stretch reflex is exerted dominantly via the gamma system, and not by altering the excitability of the large anterior horn cells.

As previously stated the static stretch reflex response is the outcome of prolonged stretch, which, since the primary annulospiral endings are slowly adapting sense organs, involves a prolonged afferent discharge. When the afferent discharge from a muscle spindle is longer in duration than a few milliseconds some additional nervous pathways must be added to the reflex already considered. These are illustrated in Fig 2, and while

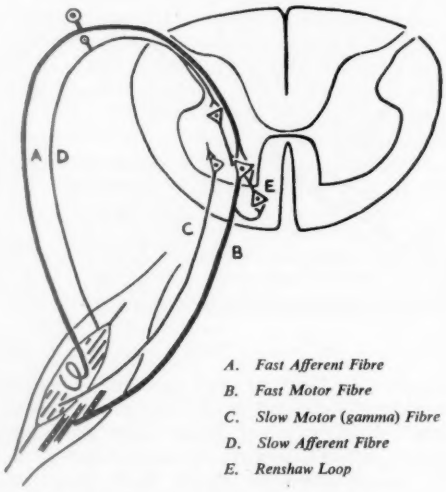

Fig 2 *Spinal pathway of static stretch reflex*

these additional pathways play a negligible part in determining the response to phasic stretch, they may so modify the reflex response to prolonged stretch as to render the static stretch reflex partially independent of the gamma system. The additions are, first, the slower conducting afferent fibres, originating in muscle spindles and reaching the anterior horn cells only through interneurons (Hunt 1954) and, secondly, the Renshaw loop (Renshaw 1941). The former, by introducing an interneuron into the reflex arc brings the static stretch reflex under supraspinal control (Eccles & Lundberg 1959) the influence of which may vary independently of the supraspinal control of the gamma system. The latter, by producing a recurrent inhibition of the motor neuron pool following the discharge of some or all the same motor neurons, may serve to stabilize – at a lower level than would otherwise occur – the prolonged motor discharge of the static stretch reflex (Holmgren & Merton 1954). That the phasic and static stretch reflexes possess the necessary anatomical connexion to allow at least their partial independence should cause no surprise to clinicians, since the independence of tendon-jerk and clinically estimated muscle tone is well recognized. Thus, although tendon-jerk and tone often change similarly – for example, hyperreflexia associated with hypertonus – hyperreflexia may be found with hypotonus, as in early hemiplegia (Buller 1957), or normal tendon-jerks may be associated with hypertonus as in paralysis agitans.

From what has been said it might be imagined that the mechanisms of the tendon-jerk and muscle tone as estimated clinically were completely understood, but several problems remain. These problems centre mainly on whether the clinical method of estimating tone by manipulating a patient's limbs elicits the static stretch reflex. While there seems no doubt that in many hypertonic states reflex electrical activity may be detected in the stretched muscles (Rushworth 1960), Weddell *et al.* (1944) demonstrated many years ago that no motor unit activity could be recorded from the stretched muscles of normal individuals who were instructed to relax during the clinical estimation of their muscle tone. More recently Hammond (1957) has demonstrated the independent control of the phasic and static stretch reflexes in man, and has shown that if a normal subject is instructed to relax, the static stretch reflex response is completely or greatly reduced in magnitude even with rapid muscle stretch. As yet unpublished observations by J Foley on the resistance to stretch of the gastrocnemius-soleus muscle group of spastic, normal and denervated subjects have shown two relevant points. Firstly, in spastic subjects the extent of the reflex electrical motor unit activity did not appear to correlate with the measured resistance to stretch either in duration or intensity. Secondly, the decreased resistance to stretch found in chronically denervated subjects could not be mimicked by acute denervation using local anæsthetics. It appears that flaccidity takes time to develop. At this point it is pertinent to enquire

what characteristics of a muscle other than its stretch reflexes are involved during stretch. Obviously the physical characteristics of the muscle will partially determine the response to stretch, but whether these properties are influenced by innervation is not in general known. However, at the purely speculative level it is interesting to note that increasing evidence is available to indicate that the innervation of striated muscle fibres may exert a profound influence on the muscle apparently independently of nerve impulse activity or acetylcholine liberation. Two examples will be given of such nervous influence. (1) Miledi (1960) has shown that during the reinnervation of a denervated muscle fibre a period exists when the hypersensitivity of the denervated fibre to acetylcholine is greatly reduced, although no effect can be produced on the muscle fibre by nerve stimulation. This effect he interprets as due to some factor other than acetylcholine passing from the nerve to the muscle fibre in the absence of neuromuscular transmission. (2) The second example concerns the slow and fast striated muscles of the adult cat. In this animal soleus is a slow muscle, its twitch contraction rising slowly – in about 80 milliseconds – to peak tension, and then as slowly relaxing. In contrast flexor digitorum longus is a fast muscle, its twitch developing peak tension in about 26 milliseconds, and then as rapidly relaxing. Buller *et al.* (1960) have shown that if the motor nerves to soleus and flexor digitorum longus are divided and then cross-united, soleus becomes a fast muscle and flexor digitorum longus a slow muscle. This effect they interpret as due to a chemical substance which passes from the nerve fibre to the muscle fibre and determines the latter's speed of contraction. Again this process is thought to be independent of electrical nervous activity. With such evidence for 'trophic' influences of nerve on muscle fibres it is not impossible to imagine that the state of innervation of a muscle fibre, and also perhaps the characteristics of the innervating motor neuron, might influence the physical properties of the muscle independently of nerve impulse activity. Any such variation would normally be summated with the stretch reflex in determining the total resistance of a muscle to stretch.

To summarize, the resistance to stretch offered by striated muscle *in situ* consists of at least two components, the first due to the physical characteristics of the muscle fibres, which may vary with their innervation, the second due to the stretch reflex. The static stretch reflex is normally under supraspinal control, and the evidence at present available suggests that when asked to relax a normal subject can suppress the reflex motor discharge. Under such circumstances the clinical estimation of muscle tone would measure chiefly the rheological properties of the fibres. If a muscle becomes denervated then, due to the absence of nervous influence over a certain time, the rheological properties of the fibres might change and hypotonus be detected clinically. With other pathological states the static stretch reflex becomes hyperactive and the reflex motor discharge cannot be volitionally inhibited. Under such circumstances hypertonus may be detected clinically, and the increased tone may be dominantly due to reflex motor unit activity in the stretched muscles.

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Tremor

Normal voluntary muscular activity in man and other mammals has for a long time been known to have a superimposed rhythmical tendency. The predominant frequency in man is about 9 per second and this was first described by Horsley & Schafer (1886).

Possible Mechanisms to Account for Tremor

One theory to account for tremor is based on the assumption that the firing of the motor cortex is modulated by the precentral α-rhythm. This has a frequency about 10/sec, but it has been shown that there is no correspondence between tremor oscillations in a limb and any electrical waveforms that can be recorded from the brain (Lindqvist/1941). Usually frequency analysis shows that tremor is slightly slower than α-rhythm and it is clear that there is no constant phase relationship. Moreover, the α-slowing which results from overbreathing is not accompanied by a change in tremor frequency.

Another explanation which has been put forward is that the spinal cord generates the rhythm of tremor. It is known that continuous medullary stimulation will drive motor neurons at about 10/sec independently of the frequency of this stimulation (Bernhard *et al.* 1947). Normal spinal motor neurons discharge at about 10/sec

under certain circumstances and it is postulated that synchronization occurring within the motor neuron pool might produce mechanical oscillations at this frequency. There is, however, evidence which does not fit this scheme. First, motor units in muscle seem to fire at from 20 to 40/sec; in normal voluntary contraction it is quite rare to find a unit discharging at less than 10/sec unless the muscle is relaxed and not exerting external tension (Bigland & Lippold 1954). Also, motor unit frequency rises as the strength of contraction increases, so that tremor would be expected to change in frequency with contraction strength. This does not happen.

A third view is that the resonant frequency of the muscle itself, or that of the limb, determines tremor. Different muscles do show slightly different frequencies but if the inertia of a limb is altered by putting weights on it the tremor rate remains constant (Halliday & Redfearn 1956).

The Servo-loop Hypothesis

The most likely mechanism giving rise to physiological tremor is to be found in the servo-loop controlling muscle length. Tremor is largely determined by oscillation in the stretch reflex system. This can be pictured as a control mechanism (like a steam engine governor or a thermostat) which gives an 'error' signal when any muscular contraction is of greater or smaller excursion than it should be (Hammond *et al.* 1956). In common with many other similar control systems, the muscle servo shows small oscillations about the mean required level.

The experimental evidence for this is based on the fact that it is possible to alter tremor rate considerably by changing peripheral conditions in the muscle. The duration of a muscle twitch can be prolonged in a muscle without influencing nervous mechanisms either in the spinal cord or in the motor nerve supply. If a human limb is cooled in a suitable water bath, twitch time increases with no change in reflex time, and frequency analysis shows that the tremor is slower. Lippold *et al.* (1957) showed that cooling the calf muscles in water at 7·5°C slowed their tremor from the normal 9 c/s rhythm to 6 c/s; moreover they recorded from m. gastrocnemius, in phase with the mechanical oscillations, bursts of action potentials which also decreased in frequency with cooling. These authors argued from these and similar findings that the effect of local cooling was upon the stretch reflex and hence that tremor was dependent upon the activity in the reflex arc.

The Effect of Deafferentation

If this explanation of the factors causing tremor is correct, it must be possible to abolish tremor by deafferenting a muscle. Lippold *et al.* (1959*a*) performed this experiment in cats. Frequency analysis of the tension records taken after the appropriate dorsal roots were cut indicates that although the general amount of muscular activity was unaltered the rhythmical tremor peak (at about 15/sec in the cat) wasc ompletely abolished. Similarly, a detailed frequency analysis of tremor in tabetic subjects showed that although there might often be more muscular activity than in normals, there was no rhythmical component with its peak at 7/sec to 9/sec (Halliday & Redfearn 1958).

Other Forms of Tremor

It is interesting to note that other forms of tremor have similar characteristics. Thus the muscular activity of shivering, thyrotoxic tremor and emotional tremor all have a similar amplitude – frequency spectrum (Lippold *et al.* 1959*b*).

Oscillation in a feed-back system tends to occur at a frequency of twice the total delay (between a stimulus and its reflex response). This fits the facts observed in the case of the muscle servo. In a human muscle such as the gastrocnemius, action potential bursts occur at 110 msec intervals. Each burst contracts the muscle which is then fully shortened 50 msec later. 25 msec after this, the spindles discharge as a result of lengthening due to passive stretching of the series elastic component. This allows 35 msec for the reflex time, a value found normally in the case of the gastrocnemius.

To keep oscillation to a minimum, engineers customarily employ 'velocity-sensitive' feed back; the main discharge of muscle spindles in fact occurs when the velocity of lengthening of the muscle is at its maximum.

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It has been clearly demonstrated by Lippold *et al.* (1957) that the grouping of action potentials in the electromyogram is directly related to the 10 c/s component of physiological tremor. They believed that the tendency to synchronization resulted from stretch reflex oscillation. I have been interested to see whether this grouping might be used to reveal stretch reflex function in various

muscles, especially those of respiration. In fact, an appearance of grouping does occur in electrical recordings from the diaphragm and intercostal muscles in conscious human subjects and in anæsthetized or decerebrate cats and rabbits. However, in the cat, I have found that the grouping persists in the diaphragm after its complete deafferentation, and in recordings from phrenic motor neurons after curare paralysis. Attempts to estimate the significance of the appearance of grouping have shown that it could occur by chance association of the firings of different motor units, unrelated but for their tendency to fire at approximately equal frequencies. That this can happen has been illustrated with an electronic model with six entirely independent units. It seems possible that chance synchronization of units can give the impression of powerful rhythmic modulation, which would be accompanied by tremor provided the frequency of firing were below the twitch fusion frequency.

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Meeting December 13 1960

Discussion on the Transfer of Drugs from the Animal Laboratory to Man

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The Design of Preclinical Animal Tests

It is only during the last fifty years that nearly all drugs have been tested in animals before their first administration to man. The two reasons why such animal tests are essential are well known. The first is the low predictability of drug usefulness: many thousands of compounds may be tested before an active drug is found. Such tests could not be done in man. The second reason is the low predictability of drug safety: a high proportion of chemical substances are poisonous; so, unfortunately, are many substances found active as drugs in animals. Careful demonstration of probable activity and probable safety is therefore necessary before any new drug is given to man for the first time.

The first administration of a new drug to man cannot be freed entirely from hazard or justified beyond doubt by any demonstration, however careful, of activity and safety in animals (Paget 1958), but care and skill can reduce hazard and doubt to low and acceptable proportions. The animal worker must accept responsibility only slightly less than that of the clinician: he must believe that his drug is likely to benefit and unlikely to harm the patient before he proposes it for trial, and his experiments must be designed to test these beliefs, and indeed to weaken rather than strengthen them.

The design of his experiments must clearly begin with a decision about his target. Since most pharmacologists who look for new drugs are industrial pharmacologists commercial interest may affect this decision, though not necessarily adversely. The interests of patient, clinician and manufacturer are identical, and are to have the best and least imitative drug possible.

This may seem to suggest that the first intention of the comparative pharmacologist should be to discover a completely new chemical with a novel mode of action against an affliction for which no drug yet exists: for example, a streptomycin or a griseofulvin. As a somewhat easier alternative he might look for a completely new chemical with a novel mode of action in an affliction already partly susceptible to drug treatment: for example a proguanil or a bretylium. He might be expected to reject the ignoble ambition of changing a methyl for an ethyl group in the structure of the twenty-fourth phenothiazine tranquillizer, and, after a few simple tests of introducing the twenty-fifth phenothiazine tranquillizer. I am not sure that this obvious and attractive decision is always correct. There are two reasons for thinking that some attention should be paid to close imitation of known drugs. The first reason is that work very unlikely to succeed must always be balanced against work more likely to succeed. The best interest of humanity would not be served if all biologists and all chemists worked on cancer: some should work on improved tranquillizers, and some, though perhaps fewer, on improved phenothiazines. The second reason is that the first drug of a new type is rarely perfect and might be perfected by near imitation. Whether these reasons are valid or not it seems inevitable that

the continued discovery of new drugs will result in a progressive though irregular decrease in the average superiority of new drugs over old drugs. It will be necessary for the animal pharmacologist, and for the clinician, continually to improve the delicacy and precision of their methods of comparing drugs.

The search for a new drug may indeed be wholly dependent on the development of a novel biological test, simulating a disease more closely than before, or based on a new clinical, biochemical or physiological discovery or theory. Advance of this kind seems likely to depend on the provision of three facilities. One is ample opportunity for fundamental research in the pharmacological laboratory: the methods, and the drugs discovered, will be no better, and certainly no more novel, than the research behind them. The second is increased research collaboration between several kinds of scientist, particularly biochemist, chemist, pathologist and pharmacologist. The order is alphabetical and has no other significance, except perhaps to suggest that biochemistry is likely to become more and more important. Such collaboration is commonplace in most industrial and state laboratories, but seems undesirably rare in many universities. The third facility is increased contact between clinician and laboratory worker. The comparative pharmacologist needs clinical knowledge that will improve his methods, and his judgment of the quality of old and new drugs.

Continual improvement in methods of evaluating usefulness and safety must reduce uncertainty; but it will never wholly eliminate it. The most important reason for this is the obvious one: no experimental animal is certain to resemble man closely in therapeutic or toxic response to any type of drug. This is true even for drugs that behave very similarly in most respects in most species: for example, a general anæsthetic. A volatile anæsthetic found in the mouse, or even in the grain weevil, will almost certainly be anæsthetic in man, but it will act on other excitable tissues than the brain: for example its effects on the heart are likely to vary from species to species in an unpredictable manner. In such circumstances one would like to rely most confidently on data from first the monkey, next the dog, next the rat, and least the rabbit, but this notion is based on intuition, not evidence. Indeed, I should think it unwise to test in man a drug that was poisonous in rat and rabbit but safe in dog and monkey unless I knew the reason for, and the clinical relevance of, the difference. No doubt the reason would usually be biochemical: for example, a substance blocking the synthesis of ascorbic acid might be toxic in the rat but safe in man and guinea-pig. The importance and value of biochemical studies of species differences cannot be overemphasized, but unfortunately adequate information is rarely available. In the absence of such information what should be done? Clearly confidence will increase as more species are tested, but after ten or a hundred mammalian species had been tried it could happen that a bird or for that matter a fish or a worm might allow improved prediction of human response. Obviously compromise is necessary, and most of us think that three or four familiar mammals are adequate.

Similar compromises can obviously be made throughout evaluation of activity and safety. The duration of a toxicity test allows a similar compromise. When animals have already been dosed for several months, prolonging the experiment is rarely likely to yield a return that justifies the additional labour. Carcinogenicity is an obvious exception and I shall return to it.

Many other experimental choices of this kind could be discussed, but once a minimal study of activity and safety has been performed by standard methods there is subsequently more to be gained from novel experiments intelligently based on the special circumstances than from multiplying the number of routine bioassays, the duration of treatments, the number of species, the number of routine biochemical tests on blood or urine, or the number of slides studied by the histopathologist.

I shall only briefly define a minimal study either of toxicity or activity. There is already a huge literature on toxicity appraisal (e.g. Barnes 1958, Barnes & Dentz 1954, Lehman *et al.* 1955, Paget 1958, Paget & Spinks 1959) and the minimal activity study would need new definition for each new drug. Moreover the two studies are not independently variable. We must do more exhaustive toxicity tests on a prolonged treatment for baldness than on a single shot treatment for lung cancer. So far as activity is concerned the minimal study should prove that the drug has a reasonable probability of benefiting the first patient to whom it is given in adequate dose, and of being better than available drugs in at least one defined respect. The minimal toxicity study should show how the drug kills, and what the major pharmacological and histopathological effects of large doses are, and these effects should be determined in at least two species, one of which is a dog, cat or monkey. The object of these studies is to define the clinical hazard, and to suggest to the clinician what side-effects should be looked for.

Three possible additions to these minimal studies need brief discussion. The first is the carcinogenicity test, the second is the experimental psychological test, and the third is research on the fate of the drug in the body.

Our ignorance of carcinogenicity is very great, and we can rarely predict this action. When this prediction is even remotely plausible the chemical must obviously be tested for carcinogenicity before the first patient receives it. Such tests require daily administration of drug to large groups of animals for very long periods, and it is usually preferable to look for a different drug. If there is no suspicion whatever of carcinogenicity it seems reasonable to propose clinical trial in the absence of evidence against this property, though there are good reasons for starting a carcinogenic test before clinical trial, and for completing it if the drug is eventually to be sold.

The experimental psychological test, for example measurement of the strength of a conditioned response is, according to some Russian authors (Smeljanskij 1959), the most sensitive and appropriate toxicity test of all. The actions of known drugs in such tests hardly justify their routine use, though they may have special relevance to car driving. Now that we all risk our lives daily on inadequate roads there are strong reasons for measuring the neurotoxicity of all drugs sent for clinical trial, though not necessarily by complicated psychological tests. We carry out these measurements routinely, using simple tests for agility and equilibrium in small animals (Riley & Spinks 1958).

The case for studying the fate of a new drug in the body is very strong. There is a considerable probability that differences in the absorption, distribution or elimination of a drug in two species will form a major part of the total difference in activity and safety between these species (many examples are given byWilliams 1959). The development of methods of estimating the drug and study of its distribution and metabolism in animals and man are important and valuable preliminaries to wide clinical test; sometimes they may show very quickly that the drug is most unlikely to succeed in man. Occasionally, but surprisingly rarely, the drug may prove very difficult to estimate by the available physical methods. Then radioactive drug might be studied, but this introduces a new clinical hazard, which needs special justification, as well as tests in animals to show that there is no dangerous localization of radioactivity in any organ.

Quantitative studies of blood concentrations in differently sized species might sometimes facilitate a most difficult calculation, that of the likely safe or active dose in man. It can usually be assumed that the transformation from animal to man may lie between the two extremes of transformation by body weight and transformation by surface area. The ratio of these two extremes may be large: 15 : 1 for mouse to man; 7 : 1 for rat to man; 2 : 1 for beagle to man. The cautious, perhaps ultracautious transformation, is by weight for activity and by surface area for toxicity. This implies that the active dose in the mouse should be less than one-fifteenth of the dose causing an unwanted effect in the mouse. After these calculations most of us end by recommending that the first dose given to man should be infinitesimal and that it should be increased cautiously until a useful or unpleasant effect is seen. Nevertheless the calculations must be made as a guide to the dose the clinician should reach in order to have a reasonable chance of observing activity, and as a guide to the dose that ought not to be exceeded.

Though I have tried to state what I believe to be generally valid principles that should guide preclinical animal tests, their rigid application to all circumstances would be foolish. Each new drug presents special problems and the most useful experimental plan will be different for each drug. Perhaps only two principles are obligatory. One is that the animal worker should never for a moment forget his responsibility to the patient and to the clinician who is to test the drug, perhaps without special knowledge of the theory and methods on which it is based. The other obligatory principle is that the laboratory worker must make all that he knows available to the clinician who wants the information. Unfortunately the clinician may often lack the time or the special knowledge, to examine all the animal evidence. This is of course an example of what is becoming only too general a problem: the increasing incomprehensibility of one specialty and one jargon to a different specialist even in a related field. The only remedy is increased interdisciplinary contact and collaboration, and I am sure that there is no field in which these are more important than the one we are now discussing.

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It is not intended to discuss the formal controlled therapeutic trial of a new drug, but the conduct of the stage before this, the initial administration to man when the safe dose is unknown and the only pharmacological data available have been got from animal experiments. New drugs which are merely slight variants of existing drugs present less of a problem and can often be tested by the physician with little disturbance of his routine hospital practice, but a completely new chemical must be approached with special circumspection.

The aim of the initial clinical investigator is to determine whether the new compound has therapeutic potentialities that make a formal therapeutic trial worthwhile, to establish a dose range and form a notion of the side-effects to be expected.

Most new chemicals are produced by commercial organizations which are so evidently expert at development research, and relatively few by academic institutions.

The problem therefore is generally that of the clinical worker who is approached by a commercial organization with a new chemical which it hopes will find a place in therapeutics and also make a great deal of money, a substantial amount of which may, in some cases, be used to improve their research facilities. Whilst the latter motive should not be overstressed, it also should not be ignored for it is capable of influencing conduct, even though this is sometimes denied.

When it is planned to give a new chemical to man for the first time every instance is different and only generalizations to which there are many exceptions can be made, but generalizations are of value if they make people think, even if only to rebut them, and I propose to offer some based on both reflection on, and experience of, this problem. As always, it is easier to ask questions than to answer them.

First the experimenter should examine the pharmacological reports of animal experiments submitted by the drug firm. If he has had no training in animal pharmacological methods he may find himself somewhat at a loss when confronted with the effect of the drug on preganglionic stimulation of the nerve to the cat's nictitating membrane, on the action of injected tyramine, on the carotid-occlusion reflex, or on stimulation of the greater splanchnic nerve. 'These results', writes Beyer (1960), 'may make sober reading for the inexperienced clinical investigator'. This is putting it mildly, and raises the question whether presenting such data to clinicians who may be competent to try a new drug but yet without experience of their significance, is really useful. To expect that all clinical investigators should know the business of the animal pharmacologist is hopeless, however desirable, and the most important thing that the inexperienced investigator should do next is to have a discussion with an independent worker who is familiar with the significance of the animal technique used. In addition discussion with a practical laboratory worker who has been personally concerned in the development of the drug is of the greatest value and I regard it as an essential preliminary. At this stage, I suggest, the 'medical representative' of the drug firm, whose main function will be in promoting formal therapeutic trials if the chemical turns out to be worth while, should not be the sole intermediary. The worker who gives the chemical to man and the animal laboratory worker have much in common and should confer directly. A discussion of what one has done and what the other intends to do can, in my experience, be fruitful, sometimes in improving the design of the proposed clinical experiment and sometimes in returning the animal worker to his laboratory to elucidate a point not previously considered.

A compound has not been properly investigated in the animal laboratory unless some effort has been made to determine not merely what it does, but how it does it. Such information, though often necessarily incomplete, helps in designing human experiments, and in controlling them should things go wrong. Experiments to determine the most suitable antidote are often important.

Data on absorption, metabolism and excretion are also valuable and such experiments should not be skimped in the animal laboratory; nor should pedestrian matters of pH of solution and the local toxicity of the compound be overlooked, for neglect of this can cause alarm during the experiment even if the end-result is no worse than a thrombosed vein in a volunteer.

If the animal pharmacology looks promising on paper, then the clinical investigator must consider the results of the animal toxicity tests. These are almost sure to have little real meaning for him except to give a feeling of security if the effective dose is only a small fraction of the lethal dose. Here the clinical investigator must rely heavily on the drug firm and can do little more than satisfy himself that the firm is scientifically competent and ethically reputable. The latter can be partly judged by whether the firm does or does not indulge in aggressive promotion in general, for firms have a character which can be judged thus, and aggressive promotion of its products implies over-optimism that is especially undesirable when it comes to presenting data for a decision as important as initial human trial. The borders where

optimism meets rashness and then becomes ruthlessness in promotion are not easily discernible.

When reading reports of toxicity tests it may be borne in mind that at least three species of animal should have been used, one of which should be the dog or monkey. Numbers of animals used must be appropriate and the chronic toxicity tests must have continued long enough, having regard to the immediate clinical intentions, and histology and urinalysis should not have been overlooked.

No clinician is likely to dispute a pathologist's opinion when he considers a substance toxic, but the clinician must, of duty, be critical of the pathologist who considers a compound safe. In this connexion we are at present faced with the problem of what should be done about a drug, Imferon, which, after proving itself as the only effective and immediately safe preparation of iron for intramuscular use, is found to be carcinogenic in animals, even if only under extreme conditions. If these animal experiments had been done before its introduction, would it have gone to clinical trial? It is hard to believe that it would. It is equally hard to dogmatize on whether it should be used any more.

Having decided to give the compound to man, the question arises whether it should be given to a normal volunteer, to a patient volunteer or to a patient who has not been consulted. On this important point it is only possible to remark that decisions will vary with circumstances. In the case of an analgesic, Keele (1959) is clearly right in stating that normal volunteers should be used, and I would add that an investigator who is himself unwilling to take drugs for symptomatic use, such as analgesics, hypotensives, hypnotics and tranquillizers, has no right to use them on others. He should also renew the experience of being an experimental subject at fairly frequent intervals. In the case of compounds for use in malignant disease it is equally obvious that patients must be used and that in some circumstances, as in psychotic states, it may even be justified to give drugs without previous discussion with the recipient. The payment of volunteers with money, or free hospitalization is accepted practice in the U.S.A., but has not found favour here; apart from the question of inducement, payment raises questions of legal responsibility. Mackintosh (1952) has pointed out that the law in England is not clear on the responsibility of an experimenter in case of accident; he incidentally quotes the maxim 'volenti nonfit injuria' and proposes as a free translation 'volunteers can't claim damages'.

Discussions on the ethics of human experimentation have been recently published by Bean (1959), Wolf (1959), Beecher (1958) and Fox (1959), and their opinions should be read and may be reflected on profitably by all who experiment on man, especially the discussion on the quality of the subject's consent where the technical aspects of the experiment are beyond his comprehension.

This raises the point of who should administer a new compound, whether the responsibility should only be taken by an independent worker or whether drug firms may employ their own staff to do it. Kohlstaedt (1960) is dissatisfied with the usual procedure of presenting the results of animal experiments to independent research workers, he finds 'many disadvantages' in it and advocates clinical research units staffed by full-time employees of the drug firms. These, he implies, are advantageous as they enable more compounds to be tested. I do not doubt this, but I do not think it is a desirable arrangement, for it is hard to believe that drug-firm employees could at all times retain a sufficiently objective and dispassionate attitude and I think that everyone, not least the clinical workers concerned, should recognize this risk. I do not imply any intrinsic moral superiority of the independent worker over the drug-firm employee; both are human, and it is, of course, not only the judgment of drug-firm employees that may be affected by factors that should be irrelevant. When a drug is thought to be ready for human trial, the professional interests of any enthusiastic research worker may warp his judgment, for, as Dr Harry Gold (1959), doyen of clinical pharmacologists, has pointed out, 'bias is a function of the human mind', and Fox (1959) has said, 'people in research do not always realize . . . that part of their vocational outfit is an extraordinary capacity for concentrating on one object at a time. When one of them tells me that a clinical experiment must be all right because he would not hesitate to do it on his wife and children, I am not, alas, at all reassured'. If this is true of many research workers, and I think it is, how much more careful must drug-firm employees be, with the inevitable pressures of enthusiastic research colleagues as well as of company loyalty; these pressures may be combated at a conscious level, but how sure can anyone be that they are not unconsciously influenced? It is hard for the enthusiast to be sure, and harder still, if not impossible, if he is employed by an organization which has as an important end the speedy commercial exploitation of a new compound. It is evident that such decisions should be taken by workers who are independent and who can be seen to be independent of even a suspicion of commercial pressure, which is why no clinical investigator should personally take money to try out a particular compound, for by this he inevitably sacrifices some of his independence, and his independence is a protection which the patient or subject is entitled to demand. Grants of money made to departments or institutions to provide facilities, and

with no conditions attached, are, of course, perfectly proper, and institutions might even charge fees in appropriate cases. In addition, Kekwick (1958) has said that 'one has only to examine the sort of publications that are appearing in countries where pharmaceutical houses are maintaining major payments to hospitals or wards in which they employ their own doctors to do their trials to see that the standard of work is extremely low'. Whether this is cause and effect could, of course, be disputed, but it is true.

Choice of dose for initial administration is arbitrary. A usual suggestion which I have adopted is to give to a man 1/8 to 1/10 of the dose in mg/kg that produces a definite effect in animals.

The conditions under which the administration should be made will necessarily vary enormously. A new drug for treating threadworms might be given orally to ambulant volunteers. A drug expected to have effects on nervous, vascular, muscular or respiratory systems would be given under laboratory conditions where continuous monitoring of ECG, EEG, EMG, pressures and movements could be made as necessary, where resuscitation equipment is available (but unobtrusive) and by a team of people who understand each other as well as the subject. In such cases intravenous administration is often desirable as giving the clearest answers and avoiding the nebulousness of awaiting absorption. As Severinghaus (1959) points out, all responses at first should be considered to be drug responses and the first administration may raise questions which the animal pharmacologist must answer before further trial is made. He also prefers that first administration be done by investigators with extensive background of research in the field and that others less experienced should only join in later. I agree with this. There is enough responsibility and anxiety on the first trial without adding unfamiliarity in the field to it.

As well as revealing all data without any exceptions, the drug firm must also reveal to whom else the drug has been offered. It is intolerable that two workers should independently take the risks of first administration of a compound. The suggestion that independent studies are valuable checks on validity is not relevant at this stage, however true it may be of later formal therapeutic trials. The investigator who undertakes first administration of a compound is entitled to apply the strictest standards to drug firms offering them, but he should also be aware of his own responsibility to these firms. If he agrees to try a compound he must be ready to do so within a reasonable time, recognizing that whilst the structure of our society continues as it is, a drug firm cannot afford indefinite delay in a competitive field. He should keep the firm informed of what he does with the drug and should agree to pass on his results to other suitable workers before he has published his own.

I hope nothing I have said will be misconstrued as an attack on any drug firms who are doing valuable research. Unfortunately some frequently seem hypersensitive to any sort of criticism, which is a pity, for a searchlight of fair criticism must, in the interest of the community, play on to their inmost motives and practices. It is vital that there should be frank discussion, for there is much at stake for the patients. The problems, especially the ethical problems, are grave. Drug firms have undertaken heavy responsibilities and must be accountable first to the community and only second to their shareholders. These problems, to which there is no easy solution, cannot be ignored or glossed over by mere protestations of good faith and responsibility.

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Section of Epidemiology and Preventive Medicine

President J A Fraser Roberts MD

Meeting November 18 1960

Paper

Epidemiological Studies in Cornwall

by E R Hargreaves MA MD (*Falmouth*)

INTRODUCTION

During the past ten years I have collected in Cornwall information on the incidence and distribution of infectious diseases and several conditions of unknown ætiology such as leukæmia, pernicious anæmia, rheumatoid arthritis and disseminated sclerosis. In this paper I shall confine myself to two diseases, namely disseminated sclerosis and tuberculosis.

DISSEMINATED SCLEROSIS

Much has been written in the past sixty years on the possible causes of disseminated sclerosis, yet we are still debating the hypotheses voiced by Clifford Allbutt (1900), namely that the disease was caused by some noxious toxin such as lead or by some unknown germ. These two hypotheses still stand, but more recently three others have entered the field:

(1) *Dietary*: Platt (1955) has suggested that the decline in breast feeding has led to the galactocerebrosides in the myelin sheath being replaced by glycocerebrosides and that this replacement may affect the resistance of the myelin. Payling Wright (1961) has shown by radioactive tracers that myelin is comparatively long lived.

(2) *Trace element deficiency*: The incident reported by Campbell *et al.* (1947), in which four out of seven workers studying swayback (a demyelinating disease of sheep due to copper deficiency) developed symptoms resembling disseminated sclerosis, stimulated investigation of a possible link between copper deficiency and disseminated sclerosis.

(3) *Allergy:* McAlpine and Compston (1952) have demonstrated in increased incidence of allergic manifestations in 250 patients investigated, compared with 250 controls. The sudden onset, remittent nature and day-to-day variation of disseminated sclerosis is reminiscent of diseases in which hypersensitivity is thought to play a part.

Prevalence

In the northern hemisphere disseminated sclerosis is a disease of temperate climates – N.W. Europe, Canada and the U.S.A. above 40° latitude. In the southern hemisphere, information is not so exact. In New Zealand, the death-rate from disseminated sclerosis is higher in the South Island compared with the North: 1·3 and 0·8 respectively per 100,000 population (Acheson 1961). In Australia, with the exception of Queensland, prevalence and latitude closely follow each other (Sutherland 1959). South Africa remains a puzzle.

Table I

Disseminated sclerosis: prevalence rates from literature

Author	*Years of survey*	*Population*	*Locality*	*Cases*	*Prevalence rate per 100,000*	*Method of assessing*
Campbell *et al.* (1950)	1946		Cornwall, Berks, Bucks and Suffolk		20	Postal survey and visits
McAlpine and Compston (1952)	1919–48	England and Wales	England and Wales		41·6	Calculated from death rates
	1931–50	Scotland	Scotland		63·7	with survival of 20 years
Pratt (1951)		41,000	Parts of Lincolnshire	14	34·0	Personal visits
Allison and Millar (1954)	1948–51	1,370,709	Northern Ireland	700	51	Personal visits
Sutherland (1956)	1953–54	231,116	Northern Scotland	154	67	Personal visits
Hargreaves (present survey)	1958	338,770	Cornwall	214	63	Hospital and G.P. records
Miller *et al.* (1960)	1956–59	1,400,000 (*a*)	Durham	662 (*a*)	47(*a*)	Personal visits (*a*)
		466,714 (*b*)			59 (*b*)	General practitioner visits (*b*)

In the Society's recent Symposium on disseminated sclerosis (*Proc. R. Soc. Med.* 1961) Dean reaffirmed his finding that disseminated sclerosis is almost unknown amongst South-African-born whites (Dean 1949).

Little was known of the distribution of this disease in Great Britain until after the Second World War. In 1931 Allison published a survey of the prevalence of disseminated sclerosis in North Wales. During the past ten years several studies have been published and I have summarized these in Table I.

Deaths

Deaths from disseminated sclerosis in England and Wales have been classified separately by the Registrar-General since 1921, but the method of coding was altered in 1939. Fig 1 shows corrected, average, five-yearly mortality rates for males and females over the past forty years. There are several points to note: (*a*) In 1921–25 the death rate was higher in men than in women. (*b*) In 1926–30 women took the lead. (*c*) In subsequent years there has been an ever-widening gap accentuated by the fact that the post-war drop in male deaths has not been accompanied by a similar drop in female deaths.

The disparity between men and women might, in part, be due to the longer expectation of life of women in the higher age groups, men succumbing more readily to bronchial carcinoma, coronary disease and tuberculosis. Evidence which tends to support this view is afforded by diabetes (Fig 2) where the changing mortality between the sexes is very similar. In pernicious anæmia (Fig 3), however, the relationship is different: the mortality rates of the two sexes have maintained the same relative position through the years. Fig 3 only goes back to 1933 as the Registrar-General has not adjusted the figures previous to that year. The rates for 1921-33, although higher owing to a different nomenclature, still retain the same relation between the sexes, quinquennial averages being:

	Male	*Female*	*Both sexes*
1921–25	57	73	65
1926–30	49	65	58

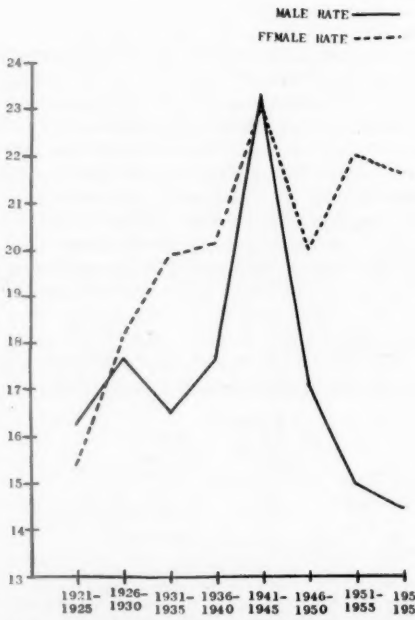

Fig 1 *Disseminated sclerosis. Deaths per million living (quinquennial averages) 1921–1958*

Fig 2 *Diabetes mellitus in England and Wales, 1901–1955. Crude death-rates per 100,000 living (quinquennial averages)*

DISSEMINATED SCLEROSIS IN CORNWALL

Information concerning the prevalence and distribution of disseminated sclerosis in Cornwall has been collected from records of deaths from the disease during the twenty-year span 1938–1957 and from an investigation of known patients during the ten-year span 1949–1958.

Deaths

Certified deaths for the years 1938–1947 were obtained by a search of the registers of deaths throughout the County. Deaths which occurred in the years 1948–1957 were collected as a progressive investigation, each Medical Officer of

Health forwarding a quarterly return of any deaths from disseminated sclerosis in his area. In all, there were 244 deaths recorded in the twenty-year period. The average population of Cornwall during this period was 332,943. The annual crude mortality rate from disseminated sclerosis was, therefore, 3·67 per 100,000.

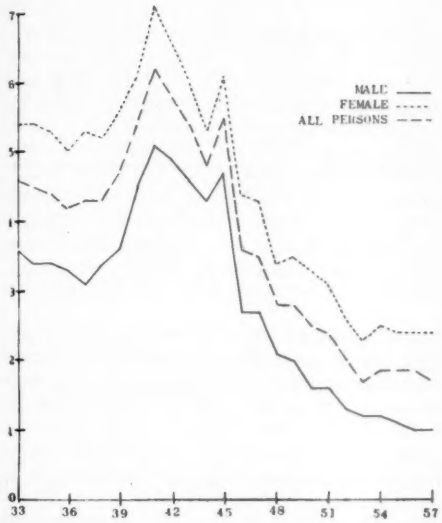

Fig 3 *Pernicious anæmia. Crude death-rate per 100,000 living. 1933–1957*

The distribution of these deaths, expressed as a percentage of total deaths from all causes in the seven Health Authority Areas of the County, is shown in Table 2 and on the map (Fig 4). A high incidence will be noted in Health Area V (largely accounted for by Wadebridge Rural District, where the rate is 110% above the mean for the County) and in Health Area VI.

Cases

A record was kept of cases of disseminated sclerosis occurring in the County during the ten-year period 1949–1958. A survey of the incidence of a non-notifiable disease is, of course, difficult, success depending on the full co-operation of the three branches of the Health Service. The investigation is explained to Medical Officers of Health and the blessing of the consultants concerned is obtained. The extent of the survey is then explained to general practitioners by letter and, where possible, at a clinical meeting. They are asked to complete a simple form giving details of patients with the particular disease in their practice and stating whether they would be agreeable for such patients to attend outpatient departments or to be visited by a consultant physician for further investigation. Dr N A Alcock, consultant neurologist, kindly agreed to help in the present investigation.

At the end of ten years (31.12.58) each practitioner was sent a list of known cases in his practice and asked to confirm that they were still alive and resident in the area, at the same time adding any further case of which he had knowledge. The

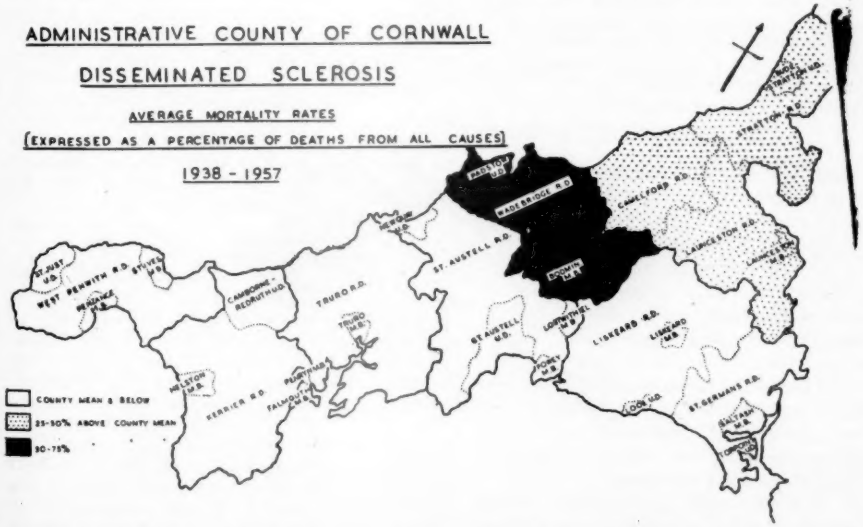

Fig 4 *Disseminated sclerosis in the administrative county of Cornwall. Average mortality rates (expressed as a percentage of deaths from all causes) 1938–1957*

Table 2

Disseminated sclerosis: deaths in Cornwall 1938–1957

	Deaths – 1938/1957				
Area	*Average population*	*Disseminated sclerosis deaths*	*Average disseminated sclerosis death-rate per 100,000*	*Average annual death-rate (all causes) per 1,000*	*Disseminated sclerosis death-rate expressed as percentage of total death rate*
I	50,483	40	3·96	14·44	0·27
II	61,296	44	3·58	14·24	0·25
III	59,575	27	2·26	13·56	0·17
IV	58,077	33	2·84	13·38	0·21
V	23,522	31	6·59	13·99	0·47
VI	29,367	34	5·79	13·29	0·43
VII	50,623	35	3·45	13·77	0·25
Total	332,943	244	3·67	13·87	0·29

Table 3

Live cases of disseminated sclerosis in Cornwall as at 31.12.58

Area	*Total*	*Population*	*Prevalence rate per 1,000*
I	31	49,530	0·63
II	35	63,870	0·55
III	48	60,960	0·79
IV	40	59,780	0·67
V	23	24,590	0·94
VI	11	28,810	0·38
VII	26	51,230	0·47
Total	214	338,770	0·63

Area I – Penzance M.B., St. Ives M.B., St. Just U.D., West Penwith R.D.
Area II – Helston M.B., Camborne-Redruth U.D., Kerrier R.D.
Area III – Falmouth M.B., Penryn M.B., Truro City, Truro R.D.
Area IV – Fowey M.B., Lostwithiel M.B., Newquay U.D., St. Austell U.D., St. Austell R.D.
Area V – Bodmin M.B., Padstow U.D., Wadebridge R.D.
Area VI – Launceston M.B., Bude-Stratton U.D., Camelford R.D., Launceston R.D., Stratton R.D.
Area VII – Liskeard M.B., Saltash M.B., Looe U.D., Torpoint U.D., St. Germans R.D., Liskeard R.D.

response was excellent, confirmatory lists having been received from all the 189 doctors practising in the County. In all, some 300 patients were collected over the ten years, but the final analysis concerns 214 patients who were seen by a neurologist, in whom the diagnosis was reasonably certain and who were known to be alive on December 31, 1958 (Table 3).

The results give a 'point prevalence' distribution in Local Authority areas as on 31.12.58 (Fig 5). The picture produced is remarkably similar to that of the deaths from the disease over the previous twenty years (Fig 4). In particular, Health Area V shows a point prevalence some 50% above the county mean and, again, it is Wadebridge Rural District, with a rate of 94% above the mean, which is responsible. This high rate is not due to the idiosyncrasy of a particular doctor, as seven practitioners notified cases in the Wadebridge Rural Area. Statistically, the figures have some significance in that the differences are more than twice the standard error.

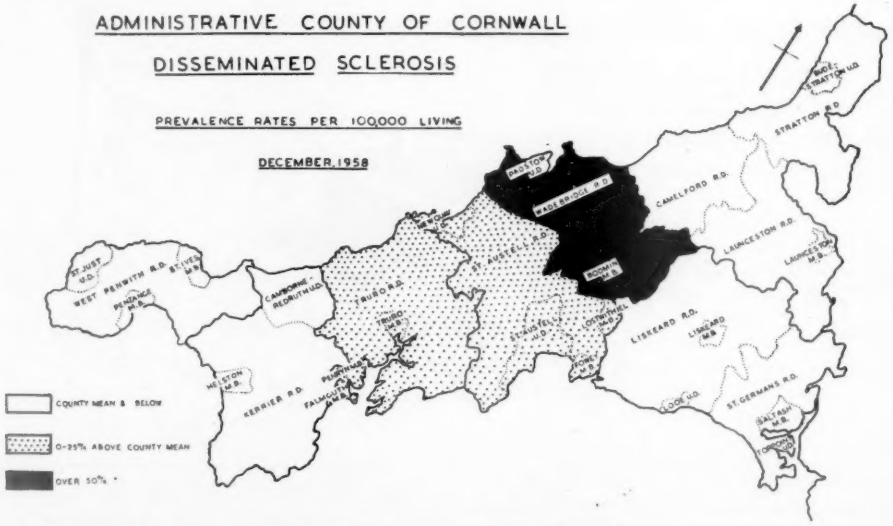

Fig 5 *Disseminated sclerosis in the administrative county of Cornwall. Prevalence rates per 100,000 living. December 1958*

Dr Harry Warren, a geologist from British Columbia, who has investigated the distribution of disseminated sclerosis in Canada in relation to lead, believes that organic lead and zinc are much more toxic than the salts of these metals and may be responsible for disseminated sclerosis. He claims that in Canada a high organic lead content of vegetation and high disseminated sclerosis rates go together (Warren 1959, 1960). In England the New Red Sandstone belt is the area where he would expect to find disseminated sclerosis. In Cornwall the geological structure he suspected was to the north of the River Camel. An analysis of root and vegetable crops for organic lead from areas in the Wadebridge District, where grouped cases of disseminated sclerosis have occurred, is being carried out by Dr K F G Hosking at the Camborne School of Mines. Antimony is being included in the analysis as lead-carrying dykes in the Wadebridge area are far less numerous than in some parts of the County, but the area is known for its deposits of antimony.

Multiple Cases

There were two instances in which both husband and wife were affected. As such occurrences are rare, I give the histories in detail.

Cases 1 and 2 A man, born in the Shetlands, went through the First World War in the Royal Flying Corps. He had several crashes but remained physically fit, apart from 1917 when he had some transient weakness in his right hand. In 1923 he had an attack of diplopia. In 1928 he went to Canada where, in 1930, he married. A year later he was admitted to Winnipeg Hospital with increasing weakness in his legs and a diagnosis of disseminated sclerosis was made. He returned to Peebles and entered the Edinburgh Royal Infirmary, where the diagnosis was confirmed by Dr J K Slater and an RAF pension was granted.

The wife nursed her husband from 1931–1942, when she was admitted to the Edinburgh Royal with diplopia and weakness in the right leg. Here, under Dr J K Slater, a diagnosis of disseminated sclerosis was made. In 1955, both husband and wife were bed cripples.

Cases 3 and 4 Mr S was born in Cornwall in 1911. He joined the R.A.S.C. in 1939, but early in 1945 at the age of 34 he began to have difficulty with balance, so much so that he could not march without bumping against his near files. He was invalided from the Army in August 1945 with a diagnosis of disseminated sclerosis confirmed at the National Hospital, Queen Square, by Dr M J F McArdle.

His wife, whom he married in 1935, was born in Penzance in 1915; there are 2 children. Apart from a visit to her husband at Newmarket during the war, she has not been away from home. Since 1945 she has had to nurse her husband in addition to caring for her two children at home.

In 1951, aged 36, she started to experience blurred vision and some months later noted weakness of her legs and, to some extent, of her arms. She was admitted to Penzance Hospital in 1952, when she was found to have exaggerated reflexes and extensor plantar responses. Her vision was still poor and she had temporal pallor of both discs. An examination of the C.S.F. showed protein – 66 mg/100 ml, globulin increased, colloidal gold 4444320000.

A curious story concerning 4 patients in one Cornish town deserves mention.

Case 5 Male, born in Cornwall in 1908, joined the County Police and for twenty years served in various parts of the county. An active sportsman, he played in the Cornwall pack before the War. In 1943, aged 35, he was stationed in the town and had a sudden attack of blindness in his left eye. The blindness, which cleared in a matter of two or three weeks, was thought to be psychological. In 1951 he developed weakness in his arms and legs, was diagnosed as disseminated sclerosis by Dr N A Alcock and died in 1958.

Case 6 Male, born in 1907, has lived in the town since he was 15. He served in the Army, being demobilized A1 in 1946 and now works in an Office. He knew Case 5 as an acquaintance more than a close friend. In 1950, aged 43, he became unsteady on his legs and in 1951 was diagnosed as a case of disseminated sclerosis. He is still at work.

Case 7 Female, born 1902, a sister-in-law of Case 6, also living in the town, developed disseminated sclerosis in the same year, 1951.

Case 8 The last of these four cases was born in 1919, in a village nearby, but subsequently lived in the town. He was in the Services during the war and on his return was employed in the same office as Case 6. He was a very close friend of Case 5. Case 8 first noticed weakness in his right leg in 1953, aged 32. This was diagnosed as sciatica, but by 1955 weakness and lack of co-ordination was marked in both his legs and a diagnosis of disseminated sclerosis was made. He is now an advanced case.

These 2 instances of conjugal patients and the little group of 4 connected patients in the same town suggest the possibility of an infection with an incubation period measured in years, ten years and six years in the conjugal cases.

Dr A M G Campbell, of Bristol, visited Iceland during the summer to obtain further information on a demyelinating disease prevalent amongst the sheep on that island. The disease is caused by a virus which has been isolated and cultured. As symptoms do not become obvious for some ten years after infection, most sheep have been slaughtered before symptoms occur (Campbell 1960). Dr Campbell has collected serum from the only survivor of the four laboratory attendants who developed disseminated sclerosis when working on swayback and, at his request, I have sent sera to Iceland from Cases 6, 7 and 8 (together

with sera from controls) for blind agglutination with the sheep virus in Iceland.

TUBERCULOSIS

Tuberculosis has a slow pathology. In consequence, the results of preventive measures are not very apparent after ten years.

In addition to general public health measures, in broad terms our policy has been to unearth the unknown patient by the examination of contacts and by mass radiography; to build up a healthy and protected teen-age population and to ensure a tuberculosis-free milk supply. Incidence maps, prepared in 1948, showed that the infection rate in the old mining areas of West Cornwall was approximately double that of East Cornwall, which is mainly agricultural. In consequence, preventive resources, particularly mass radiography, have largely been concentrated in the west.

Seven full-time Tuberculosis Health Visitors were appointed in 1948, and the contact net has gradually been spread wider. In 1948, there were 3 contacts examined per case and in 1959 there were 10 contacts examined per case. The histogram (Fig 6) shows progress to date. Some improvement is noticeable in the early 1950s but for the past four years, the incidence and mortality show little change.

Table 4, giving the bi-annual average notification in age groups, 1948–1959, shows a reduction of 62% in the 15–24 years age group, a satisfactory reduction in the 25–44 years and 0–14 years age groups, but a rise in incidence in the 45+ age group (Fig 7). When analysed in sexes it will be seen that notifications in men in the 45+ groups have risen by 105% and in women by 30% (comparative figures for England and Wales in the 45+ age group: men, a drop of 1%; women, a drop of 10%) (Fig 8).

This drop in notifications is not very encouraging, but perhaps a more reliable indication is to be found in tuberculin sensitivity rates (Table 5).

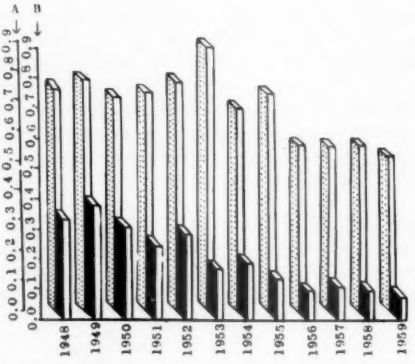

Fig 6 *Pulmonary tuberculosis. Notifications and deaths. Rate per 100,000 population. 1948–1959 A. Notifications, B. Deaths*

Table 4

Pulmonary tuberculosis: Notifications by age and sex. Rates per 100,000 population 1948–1959

Age Groups	0–14			15–24			25–44			45+		
	M	*F*	*Total*	*M*	*F*	*Total*	*M*	*F*	*Total*	*M*	*F*	*Total*
Sex and population (1951 census)	35,777	34,695	70,472	23,879	21,518	45,397	45 618	48,514	94,132	59,503	75,938	135,441
1948 Total cases	19	23	42	78	58	136	95	90	185	70	29	99
1949 Annual rate	26·5	33·1	29·7	163·3	134·7	149·8	103·0	92·9	97·7	58·8	19·0	36·2
1950 Total cases	28	19	47	54	69	123	96	94	190	104	25	129
1951 Annual rate	39·1	27·3	33·3	113·7	160·3	134·4	105·2	96·8	100·9	87·4	16·4	47·2
1952 Total cases	25	24	49	72	88	160	114	104	218	114	35	149
1953 Annual rate	34·9	34·5	34·7	150·7	204·4	176·2	124·0	107·2	115·8	95·8	23·0	54·6
1954 Total cases	37	25	62	52	64	116	96	68	164	111	47	158
1955 Annual rate	51·7	36·0	43·9	109·0	148·7	127·8	105·2	69·8	87·1	93·2	30·9	58·3
1956 Total cases	19	16	35	31	38	69	60	68	128	123	36	159
1957 Annual rate	26·5	23·5	24·8	64·9	88·3	74·9	65·7	70·0	67·9	103·3	23·7	58·3
1958 Total cases	16	10	26	20	29	49	62	59	121	144	40	184
1959 Annual rate	22·5	14·4	18·4	41·8	69·7	55·1	67·9	61·8	63·7	121·0	26·3	67·9
% Change – Cornwall 1948/1958	−16	−56	−38	−64	−56	−62	−35	−34	−35	+105	+40	+85
% Change – England & Wales 1948/1958	−49	−49		−54	−62		−45	−47		−1	−9	

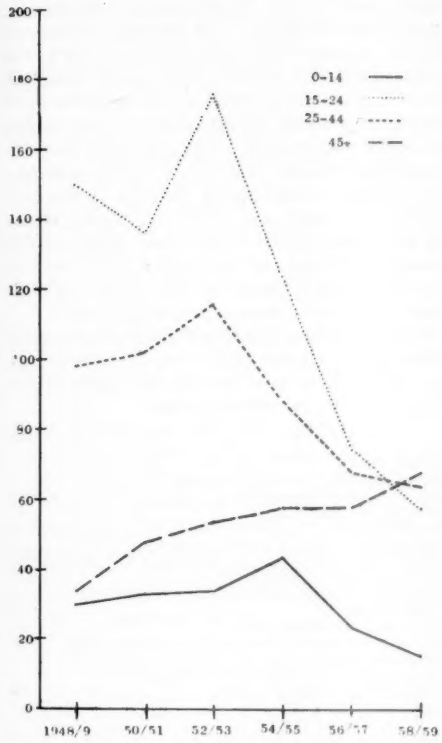

Fig 7 *Tuberculosis. Notifications 1948/59. Bi-annual rate per 100,000 by age groups*

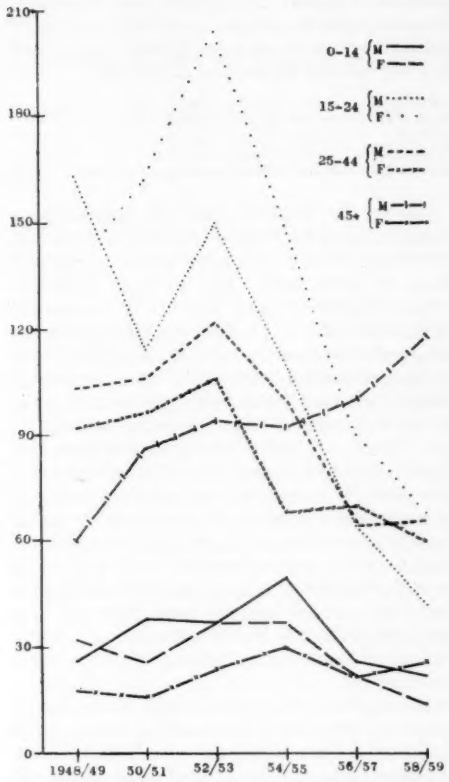

Fig 8 *Tuberculosis. Notifications 1948/59. Bi-annual rate per 100,000 by age and sex*

Table 5
Tuberculin sensitivity rates

	1954–55	1959
Cornwall	19·5	14·2
West Cornwall	23·8	15·8
East Cornwall	14·1	12·4

Approximately 4,000 children per year were tuberculin tested using 10 i.u. of tuberculin (0·1 c.c. of 1/1,000). From this it can be concluded that the amount of active disease at large in the community has been greatly reduced, particularly in West Cornwall.

Protection of School Children

The scheme for tuberculin testing and BCG vaccination of 13-year-old children started in 1953 and was well received. Table 6 gives a summary of this work. It will be noted that half the notified cases of tuberculosis have occurred amongst those who slipped through the net.

Table 6
Tuberculin Testing & BCG vaccination: School children (13 yrs) 1953–1959

		Notified cases of tuberculosis
No. of children eligible	27,870	56
No. of children absent or refused	5,049	27
No. of children tuberculin tested	22,821	
Percentage tested	82%	
No. of children tuberculin +	4,198 (18%)	28
No. of children tuberculin −	18,564	1
No. of children BCG vaccinated	18,219	1

Bovine Tuberculosis

This plays an ever decreasing part in human disease. It is possible that tuberculosis-free herds may be susceptible to infection from human sources. An incident illustrating this possibility occurred recently. Cornwall is now a specified area, which implies that all dairy herds are subject to a tuberculin test and all reactors must be slaughtered. In the autumn of 1959, I was

approached by Mr L E Perkins, the Divisional Veterinary Officer, concerning the high number of tuberculin reactors on a small dairy farm owned by a Mr W. The figures are as follows:

August 1958	6 out of 20 cattle reacted
March 1959	4 out of 28 cattle reacted
July 1959	2 out of 38 cattle reacted
October 1959	7 out of 52 cattle reacted
January 1960	10 out of 40 cattle reacted

All the 29 reactors had, of course, been slaughtered but Mr Perkins was unable to explain the persistently bad record and wondered whether the cattle were being infected from a human source. Enquiry revealed that Mr W's son, aged 27, was admitted to a sanatorium with cavitation and positive sputum on October 30, 1959. Of the contacts, the father, who suffers from bronchitis, refused to submit himself for examination until his son had returned from hospital, maintaining that, should we find anything in his chest, we would forbid him to continue the dairy farm and there would be nobody left to look after the cows. He was equally emphatic in forbidding his wife, blind and housebound, to be examined. All the other contacts were examined, among them a married daughter who had a positive sputum and cavitation. A last appeal was made by the Veterinary Officer to Mr W to have an X-ray for the sake of his cattle, but the old man remained unmoved.

Cultures from the sputum of both these cases of pulmonary tuberculosis showed their infections to be of bovine type. These cultures, together with the culture from the slaughtered cows, were sent to the Ministry of Agriculture Laboratory, Weybridge, and to the Public Health Laboratory, Exeter, for comparison. Dr Brendan Moore of Exeter reported that subcultures of both the human and the bovine strain gave identical dysgonic growth on various media and that both caused generalized tuberculosis in guinea-pigs and rabbits with death of the rabbits in the fifth week after intravenous injection. The intravenous test in rabbits differentiates between bovine and human type strains, only the bovine type producing this rapid generalization and death of the animal. The tuberculin test history of the herd in question strongly suggested that the bovine type infection spread from man back to the cattle.

This has led to a new approach. The Veterinary Officer notifies me of herds with abnormal reactors and I have now one further herd whose human contacts we are examining.

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Meeting October 21, 1960

A Discussion was held on **The Nature of Essential Hypertension;** the opening speakers were Professor Sir George Pickering and Professor Sir Robert Platt.

Section of Dermatology

President Hugh Gordon MC FRCP

Meeting October 20 1960

Cases

Melkerson-Rosenthal Syndrome

R J Cairns MRCP

Mrs K B, female, aged 48. Housewife.
History: First attack of left facial palsy occurred at the age of 12. Four years later the right side was affected and ten years later there was a recurrence on the left. Since then she has had attacks of œdema of the upper lip, nose and buccal mucosa, usually commencing overnight and lasting about two weeks. The attacks are sometimes painful, frequently associated with herpetic blisters over the area involved, and are sometimes provoked by a cold draught. The swellings are preceded for a day or two by frontal headaches with nausea. There is no visual disturbance and no swelling of the eyelids. There is no alteration in sense of taste or hearing. Occasional vasospastic attacks in fingers in cold weather.
Clinical findings: Residual left facial weakness, with œdema of upper lip and lingua plicata.

Investigations: Full blood count and E.S.R. normal. Serum proteins increase in β-globulin (1·27 g/100 ml) and in γ-globulin (1·34 g/100 ml). Cold agglutinins and cryoglobulins – none detected. Ice applied to the upper lip for 60 seconds – nothing abnormal noted. X-rays of chest and fingers normal.

Histology (lip and tongue) (Dr H Haber): The sections do not show any signs of Meischer's cheilitis. The corium exhibits a non-specific inflammatory reaction. Small vessels appear to be dilated and engorged.

Comment: The characteristic features of Melkerson-Rosenthal syndrome are present in this case. The facial palsy in this syndrome is often bilateral and recurrent, commencing even in childhood, and it may precede or coincide with the onset of œdematous attacks. The œdema usually affects the upper lip and cheeks. In this patient it also affects the nose and buccal mucosa. Some cases are precipitated by cold and in the early stages the swelling may involute completely between attacks. Associated symptoms include migraine, vertigo, tinnitus and lachrymal hypersecretion. This patient shows lingua plicata as described by Rosenthal in 1931.

The association of facial palsy and œdema is thought to be due to autonomic dysfunction. A significant proportion of patients with Melkerson-Rosenthal syndrome have migraine and perhaps sympathetic or para-sympathetic over-activity might induce vasospasm and neural ischæmia. Alternatively, a later phase of vasodilatation with œdema might provoke compression of the facial nerve in the Fallopian canal. Presumably, the cutaneous swelling in these cases is due to vasodilatation. In this patient exposure to a cold draught or the application of ice failed to produce swelling. It is hoped that when spontaneous swelling appears selective blocking of the sympathetic and para-sympathetic pathways might help to clarify the problem. Unfortunately, the anatomical pathways to this part of the face are not at all clear. It might be significant that following bilateral stellate ganglion block the central area of the face continues to sweat. It might also be interesting to try the effect of ergotamine on the œdematous attacks.
The œdema present to-day appears to be persistent. We have not, so far, seen her during one of the acute attacks. She has noticed herpetiform vesicles after each episode; whether they are herpetic or not I do not know.

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Dr C H Whittle: Could you not find this out if you looked for the virus?
Dr R J Cairns: Yes.

Lichen Myxœdematosus

O L S Scott MRCP

This is the case of the retired nursing sister aged 65. She has had these firm, waxy flesh-coloured papules, measuring about 1–3 mm diameter on the

upper limbs and neck for the past nine months. These papules are set in a background of hard skin, almost sclerodermatous in texture (Fig 1). Histology shows increased deposits of mucin amongst essentially normal collagen and elastic tissue in the upper dermis. These findings are consistent with a diagnosis of lichen myxœdematosus (or myxœdema papulosum, papular mucinosis).

Comment: The word myxœdema was coined in 1878 by Ord to describe non-pitting swelling of the skin in association with deficiency of thyroid secretion. The terminology is confused since the word is used in two senses, viz. the sense commonly used in general medicine to describe the state of hypothyroidism and the literal sense used by dermatologists to describe mucinous infiltration of skin.

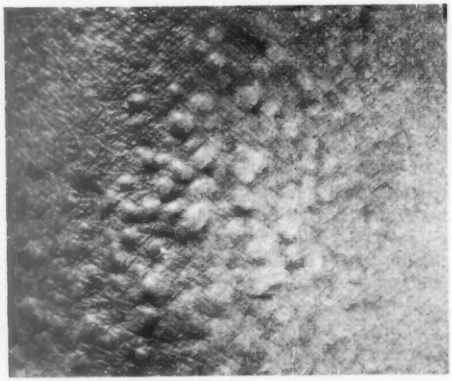

Fig 1 *Lichen myxœdematosus: area taken from right wrist*

Green & Freudenthal (1948) showed a case very similar to this at the Section Meeting in March 1947 under the title myxœdema papulosum. Speaking of myxœdema, Dr W Freudenthal grouped cases into three: (1) Generalized myxœdema, e.g. cretinism. (2) Pretibial myxœdema of Grave's disease, and (3) Atypical myxœdema of Jadassohn-Doessekker, with no thyroid abnormality. This case we have seen to-day is in this third group.

The cause of the condition is unknown. In some cases regression of papules which have been injected with hyaluronidase has been noted, if the area is covered with a pressure bandage. However, the injection has to be made with some force and is uncomfortable, and has not been tried in this case.

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Reticulohistiocytosis: Resembling Xanthoma Disseminatum

B Woods MB MRCP and C H Whittle MD

T P, male, aged 42. Clerk.

History: For just over a year papules rather like hæmangiomata have been appearing on most parts of his body, beginning in the axillæ where they are now most numerous. At first they were raised, firm and violet-red in colour, but later became flattened and brownish. A few on the face have disappeared spontaneously and several have been destroyed by electrodiathermy without recurrence. His general health is good, and he has had no polyuria, angina or arthritis. No relatives had skin lesions, diabetes or significant cardiovascular disease.

Clinical findings: Most of the lesions are brownish-red, shiny, circular, dome-shaped papules from 1 to 7 mm in diameter, and some have faint erythematous haloes. In the inguinal region some are yellower, and the older papules in most areas have become smaller and faded to yellowish brown. There is no tenderness or itching. The papules are widely dispersed but are absent from the palms, soles and scalp. They are rather more numerous in the flexures of the elbows, axillæ and groins. Two nodules on the tongue are the only lesions found in the mouth and upper respiratory tract. General examination is normal except for a blood pressure of 170/95–175/105.

Investigations: Hæmoglobin, white cell count and E.S.R. normal.

Plasma proteins (total and electrophoretic pattern) normal.

Plasma cholesterol 30.9.60: 394 mg per 100 ml. 5.10.60: 340 mg per 100 ml. 14.10.60: 215 mg per 100 ml.

Total lipids: 0·62 g per 100 ml. Phospholipids: 10·0 mg per 100 ml. Lipoprotein electrophoresis: normal. Skiagrams of chest, skull, spine, pelvis and hands: normal. Electrocardiogram: normal.

Histology (Dr A M Barrett): This nodule in the upper corium is of granulomatous appearance and contains numerous rather large irregularly shaped cells with one or several vesicular nuclei, conspicuous nucleoli, and eosinophilic cytoplasm. These cells resemble large histiocytes. Frozen sections show that many of them contain many small droplets of anisotropic lipoid material. I have not seen any typical foamy xanthoma cells in the paraffin sections.

Besides the histiocyte-like cells, there are a considerable number of neutrophil leucocytes,

lymphocytes and plasma cells, and a few eosinophils. There is apparently some fibrosis in and around the nodule.

The findings are similar to those of xanthoma disseminatum as seen in some cases of Hand-Schüller-Christian and Letterer-Siwe diseases.

Biopsy of an older papule showed an ill-defined lesion with less infiltrate and increased fibrosis. There were still no typical xanthoma cells.

Comment: The morphology, distribution and histology suggest either xanthoma disseminatum (regarded as a variety of 'histiocytosis X') or reticulohistiocytosis. Hypercholesterolæmia has rarely been described in xanthoma disseminatum (Koch & Lewis 1956, Smith 1959), but the mild degree found in the present case is not uncommon in reticulohistiocytosis (Warin *et al.*, 1957). However, only one of the 16 cases reviewed by Warin *et al.* developed a rash before bone or joint changes appeared and the distribution of papules in the present case is unusual. On the whole the histology seems more like that of reticulohistiocytosis, and we think the better prognosis of this disease is probably justified.

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Dr H Haber: The nodule is composed of three types of cells – (1) large bizarre mono- and multi-nuclear cells; (2) lymphocytes; (3) polymorphs. The large cells, which I do not think are xanthomatous, have opaque purple cytoplasm and vesicular nuclei with large nucleoli and are phagocytic, polymorphs and lymphocytes having been engulfed by them. A few cells contain a brown pigment.

The lesion I think is reactive and is perhaps a type of reticulohistiocytoma. In the absence of joint involvement the condition may resolve spontaneously. A case I saw a year ago with lesions on the face and trunk cleared up in six months.

Dr Warin: I have no doubt that this is a case of reticulohistiocytosis. The eruption is typical but there is no joint involvement. In the literature there are a number of cases which started off with the rash alone and later developed joint disturbance.

Dr D E Sharvill: I showed a case before this Section in January 1958 which was similar to those described by Caro, Senear, Warin and others. The lesions were distributed over the ears and hands especially, which is typical, and they were much more uniform in appearance, firm and skin coloured or reddish. They differed histologically in several respects from the slides shown of the present case. It is true that these cases ultimately burn themselves out and may eventually present a very nondescript appearance, but I do not think that the present case belongs to the same group at all.

REFERENCE
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Dr B C Tate: I do not think this is anything like the so-called reticulohistiocytoma. I agree with what the previous speaker said about the skin coloured waxy-looking nodules occurring on the ears and hands, and tending to be grouped, whereas these are discrete, nor do I think the histology is the same. The characteristic feature is an enormous number of giant cells. If you look down the microscope it hits you in the eye. I think it is quite a different thing.

Dr P Smith: I agree with Dr Tate and Dr Sharvill. As Dr Tate said, the histology of reticulohistiocytoma is remarkable for the enormous number of multinucleated cells.

Dr H Haber: If you look at the section, you will find enormous numbers of giant cells.

Dr C H Whittle: I originally labelled it reticulosis. I was rather frightened off this diagnosis by the raised blood cholesterol. Now I lean more towards reticulohistiocytosis, with a slightly better prognosis.

The following cases were also shown:

Poikiloderma Congenita (Thomson's Syndrome) associated with Recurrent Blisters on Feet and Spasticity of Legs and Arms
Dr R P Warin

(1) **Pseudo-acanthosis Nigricans**
(2) **Porphria Cutanea Tarda**
(3) **Rheumatoid Arthritis with Papulonecrotic (Arteriolar) Lesions Fingers and Elbows**
(4) **Pityriasis Lichenoides Acuta**
Dr R J Cairns

(1) **Two Cases of Erythrocyanosis Frigida Crurum Puellarum**
(2) **Dermal Atrophy**
Dr P Hall-Smith

Mast Cell Nævus
Dr B Russell

Acrodermatitis Chronica Atrophicans
Dr N A Thorne

Pemphigus Foliaceus
Dr N S Saha (for Dr E Colin-Jones)

Follicultis Ulerythematosa Reticulata
Dr D Sharvill

Meeting November 17 1960

Cases

Lipoid Proteinosis (Urbach-Wiethe) (Hyalinosis cutis et mucosæ)

M A Cowan MB MRCP (for H R Vickers MD FRCP)

M B, aged 43. Housewife.

History: Inability to cry at birth, and subsequent hoarseness. 12 years of age: development of lesions of left shoulder, neck, and elbows. 1956: diagnosed as having akinetic epilepsy, controlled by Epanutin. 1958: referred to ENT Department with hoarseness, and from there to Department of Dermatology. Had increased tendency to bruise with a positive tourniquet test and menorrhagia. Corticosteroid therapy for eight months with improvement of voice, skin lesions and disappearance of bruising tendency. August 1960: painless swelling of left submandibular gland for one month. Hoarseness and skin lesions have slowly progressed since onset except during corticosteroid therapy. No history of consanguinuity, but her mother has diabetes mellitus.

Clinical findings: Diffuse non-scarring alopecia, particularly of occipital region. Face waxy and wrinkled with a mauve atrophic patch of right side of forehead, pearly bead-like lesions of margins of upper eyelids and fissured infiltrated plaques of angles of mouth. Tongue normal. Yellowish follicular papules with perifollicular atrophy of neck and upper arms. Hyperkeratotic plaques of both elbows with warty excrescence on the left. Infiltrated lesion of left shoulder and gluteal cleft. Infiltrations of pharynx. Considerable thickening of both vocal cords with pallor, scarring and some proliferation posteriorly.

Investigations: Blood count, platelets, bleeding time, capillary microscopy, urine, Wassermann and Kahn, plasma proteins, blood lipoid phosphorus, normal.

Skull X-rays: Bilateral bean-like calcification in temporal lobes, probably medial to posterior horns of lateral ventricles.

Electro-encephalogram: normal.

Biopsies of skin and larynx histologically similar. They show clumps of hyaline, PAS positive material in the dermis with perivascular and periglandular deposition. (The perivascular material appears to be replacing the mucous membrane.) The elastica is degenerate and reticulin absent in these areas. Thick fragmented clumped areas of elastic outside the hyaline material.

Comment: This patient presents a classical picture of lipoid proteinosis with a new feature of increased bruising tendency. The histological findings so far as they go, support the hypothesis that this is an infiltrative rather than a degenerative condition.

Dr H R Vickers: I first saw this patient some three years ago and she was referred to me from the ENT Department. I thought that she probably had pseudoxanthoma elasticum but the correct diagnosis was made by the pathologists on the biopsy from the skin of the side of the neck. I mentioned this case in my Watson Smith lecture.

Dr G B Dowling: According to Scott & Findlay (1960) who have studied the literature very fully this may well be the first case to be presented in Great Britain. These authors have recently collected 27 South African cases and they point out that like two other inherited diseases, porphyria and pseudoxanthoma elasticum, the incidence in relation to population is very high indeed. The South African cases have occurred in 18 white families of whom 17 bear Africaans surnames, and 1 coloured family. They believe that the anomaly was probably imported from Germany at an early stage of the white settlement in South Africa.

In a personal communication Dr Findlay has informed me that none of the South African cases, of which the first was reported in 1948, has died.

REFERENCE
Scott F P & Findlay G H (1960) *S. Afr. med. J.* **34**, 189

Dr C D Calnan: Last week I saw a severe example of this condition in Professor Orbaneja's clinic in Madrid. The patient was a child of about 8 or 9 and the whole of her face showed intense reddish yellow infiltrate. It is possible that light had something to do with it.

Professor J T Ingram: I saw Urbach's original case in Vienna in 1935. There was a positive family history. I understand there is no family history in this case? The condition is described in a recent book by Fleischmayer.

Dr J J Jacobson: We see quite a number of these cases in South Africa: the pathologist's report always makes the diagnosis very soon. They include very young children, and often there is a familial pattern.

Psoriasiform Dermatosis associated with Bizarre Metabolic Abnormalities

Maurice Garretts MRCP (for Professor C E Dent)

S A M, female, aged 12. Schoolgirl.

History: This girl was referred to University College Hospital by Dr Patrick Montgomery, to whom we are most grateful for the opportunity to

study this patient. She had knock-knees when aged 2, and at this time she suffered from infantile eczema. Since the age of 4 she has had dry and scaly patches on her skin, and these became a severe eruption six months ago. One year ago she had two epileptiform convulsions for which she was given phenobarbitone. She was sent to see Dr Montgomery six months ago with a rash which was thought to be psoriasis, and at this time the signs of latent tetany were elicited and she was referred to the Metabolic Unit at University College Hospital for further study. She was then regarded as a possible case of eruption associated with hypocalcæmia.

Clinical findings: There was a widespread eruption consisting of psoriasiform plaques 2–4 cm in diameter, mainly on the trunk. In addition there were large areas over the upper trunk and back showing the most pronounced follicular hyperkeratosis (Fig 1). The Chvostek sign was easily

Fig 1 *Case S A M: skin below shoulder, taken in horizontal position, showing psoriasiform plaques and follicular hyperkeratosis. The largest plaques measured about 4 cm in diameter*

elicited. There was bilateral genu valgum with intermalleolar separation of 4 in. She was on the 16 percentile for height. She was plump and healthy otherwise.

Investigations: Serum calcium 4·9, phosphorus 9·6 mg%. Phosphatase 42 K-A units. Electrolytes normal. Urea 18 mg%, urea clearance 114%. Twenty-four-hour urine calcium 14 mg, phosphorus 619 mg. Urine S.G. range 1004–1020. Glucose tolerance test: slightly flat curve obtained. Fat balance 98% absorption. Xylose absorption test normal. Vitamin A absorption normal. Dark adaptation test impaired, compatible with mild vitamin A depletion (Dr G Arden). Fasting vitamin A level 90 and 130 i.u./100 ml (low normal). EEG: widespread high voltage activity in a wide range of frequencies.

Skin biopsy (Dr A Jarrett): The histology of the follicular lesions shows a parakeratotic intrafollicular keratinization. The psoriasiform plaque-like lesion showed a diffuse parakeratosis with a thickened epidermis and is indistinguishable from psoriasis. However, these lesions are quite different in their development. In psoriasis the follicles are the last region to be affected by the parakeratotic process, whereas in this case they are the first to show the change. This strongly suggests that the lesions in this case are those of a primary avitaminosis A of the skin.

Comment: The investigations yielded very puzzling results. Because she presented with latent tetany and an eruption closely resembling that seen in vitamin A deficiency, it was tempting to consider that she might have steatorrhœa with tetany, considered by some to be due to inability to absorb vitamin D and the follicular hyperkeratosis of phrynoderma due to the inability to absorb vitamin A. Her history of knock-knees together with poor linear growth suggested mild rickets. The rickets was not gross enough to show any clear X-ray changes, but the high alkaline phosphatase was very suggestive. In addition to these factors she had an eruption similar to that associated with vitamin A deficiency, but occurring in the presence of only low normal plasma vitamin A levels. Her diet was normal and there was an adequate intake of vitamins A and D. We assumed that she must have occult steatorrhœa, or else something very complicated which we had not heard of before. The interpretation of her condition was further complicated by her gross biochemical hypoparathyroidism, which undoubtedly explained her tetany and probably her epilepsy of one year ago.

She was put on a fat balance regime and during this time we confirmed that she had abnormal dark adaptation, as in a mild case of vitamin A deficiency. The skin biopsy material was found to be consistent with that diagnosis, and we are most grateful to Dr A Jarrett for carrying out the histological studies.

She had an abnormal EEG tracing and all other tests of renal function and electrolytes &c. were normal. The fat balance came back normal. While we recovered from the surprise, further tests of renal phosphate threshold were made and these fully confirmed a high threshold typical of hypoparathyroidism.

Recently we have recorded cases of skin disease in which the rash was directly related in severity and onset to the serum calcium level (Dent & Garretts, 1960). These cases were in the main eczematous. It was nevertheless planned to treat this girl with vitamin D only in order to see how far improvement in her serum calcium level might affect her skin as well as her tetany. After giving a loading dose of dihydrotachysterol (DHT), she was put on a maintenance dose of 2 mg/day. She responded rather slowly and her calcium level slowly rose to normal, while the phosphorus fell, this latter being shown to be due to a fall in her renal phosphate threshold to nearly normal. This response is quite typical of that which occurs in hypoparathyroidism. During this time her phosphatase level fell, thus confirming that her raised phosphatase was due to rickets and not to a hepatic cause.

During the period of treatment with DHT her skin definitely became worse, thus confirming that the eruption was not due to hypocalcæmia. It was, however, interesting to note that local treatment during this time of a small scaly patch with vitamin A (50,000 i.u./ml), resulted in a definite improvement of the eruption where the vitamin A oil was applied. There was no improvement of another scaly patch treated with the solvent oil only.

It was next decided to discover her response to vitamin A while her serum calcium level was maintained at normal levels with appropriate maintenance doses of DHT. A vitamin A absorption test was first of all carried out and this showed normal results, a further point against the possibility of steatorrhœa. She was then given vitamin A 50,000 i.u. daily by mouth, and there was little doubt that her skin began to improve, especially on the trunk, after two weeks' treatment. First the follicular lesions disappeared and later the large psoriasiform lesions began to improve, shedding their scales and leaving normal skin underneath. Her dark adaptation test became normal.

Since her EEG was still abnormal after raising her serum calcium level to normal, she was presumed to have an underlying irritable focus which had been triggered off to produce epilepsy by the low serum calcium. It was decided to stop her phenobarbitone.

She was discharged from hospital on May 29, 1960, and she was sent out taking 2 mg daily of DHT, and as we were impatient the dose of vitamin A was raised to 250,000 i.u. daily. On follow up her plasma calcium was satisfactorily maintained at normal with DHT. A close watch was kept on her plasma vitamin A levels. They had not risen one month afterwards so the dose was increased to 750,000 i.u. daily. Her skin was quite normal at this stage, although there were still marked psoriasiform patches in her scalp. On October 3, 1960, she presented the features of vitamin A intoxication with a very high plasma level of vitamin A. The vitamin A was stopped and she has not been put back on it. Her calcium, phosphorus and phosphatase levels remain satisfactory and she has had no further tetany or epilepsy.

Professor C E Dent: I wish to support Dr. Garretts' remarks to the effect that the patient had, associated with the dermatosis, clear evidence of hypoparathyroidism, of mild rickets and signs of vitamin A deficiency. We controlled her treatment closely in our Metabolic Ward. Her response to vitamin D was that of the state of hypoparathyroidism; her plasma calcium rose, the phosphorus fell and the renal clearances showed an abnormally low clearance before and a normalization after the vitamin D was given. The evidence for rickets was in her history of knock-knees and high plasma alkaline phosphatase levels, which latter became normal as the vitamin D was given in doses sufficient to control the hypoparathyroidism. The signs of vitamin A deficiency comprised the clinical signs of the dermatosis and the skin histology which was consistent with this diagnosis. Of further importance was the result of loading with large doses of vitamin A, no other change of treatment occurring; her dark adaptation became normal and the dermatosis improved in the most spectacular manner. This latter is now beginning to return since we have temporarily stopped the vitamin A.

Clearly the signs of vitamin A and D deficiency in this child (if you accept this evidence) have arisen in the presence of normal dietary intakes of these vitamins. The child appears, therefore, to have a higher than normal requirement since supplementation by large doses has corrected the deficiencies. The simplest plausible mechanism for this is presumably a metabolic disturbance in the body leading to excessive rate of destruction of the vitamins, or to an inability to act properly on their target organs. The same disorder may well have caused her own parathyroid hormone to be ineffective, and it would be most fascinating if eventually there could be discovered a common pathway of metabolism of these three factors, so essential to normal development. This patient is presented in the hope of stimulating such thoughts, and perhaps to direct future research along these lines. We have not yet come across a similar patient in the literature. It is relevant to point out, however, that there are already known to be many complicated syndromes in which apparently disordered function of the parathyroid glands (hypo- or hyper-) is associated with other metabolic defects.

We are in the course of preparing a fuller paper on this child for publication elsewhere.

REFERENCE

Dent C E & Garretts M (1960) *Lancet* i, 142

Dr I B Sneddon: We have a similar case in a woman of 51, who eleven years ago had a total thyroidectomy. Within weeks she developed widespread psoriasis and

this was associated with a low serum calcium as her parathyroids had been removed at operation. The psoriasis varies directly with the level of serum calcium, clearing if it returns to normal.

She has also had an epileptiform attack and an abnormal EEG when her serum calcium has been low.

Dr H R Vickers: I well remember the case described by Dr Sneddon since she was under my care when I was in Sheffield. I saw a second similar case three years ago who was referred to me by Professor Witts. He was a man with very widespread psoriasis which followed thyroidectomy and he was found to have hypoparathyroidism with low serum calcium. He was treated with calciferol, the serum calcium returned to normal and the psoriasis cleared. I would like to discuss the local application of vitamin A, since vitamin A in an ointment base will act as a keratolytic agent and beneficial results when used on scaling skin may be due not to any specific action of vitamin A but to the non-specific keratolytic effect.

Hyperkeratotic Follicular Plugging with Alopecia Totalis

R D Sweet MRCP

Male aged 61.

Has had a dry skin all his life with scaling on the extensor aspects of arms and legs.

Family history: Negative. 8 sibs all unaffected.

History: Thyroidectomy 1942: Cerebral thrombosis 1954 from which he has recovered completely, apart from some minor trouble with his speech.

Three years ago he developed a hypostatic eczema on his right lower leg which became severe just under two years ago, and at that time he probably had some papular eczema on his back. Since then the skin of his trunk has appeared ichthyotic also.

One year ago the sides of his face and temple regions of the scalp began to be affected, as at present, and the whole picture became fully developed within two or three months. He does wonder, however, whether further areas are gradually becoming involved lately.

Six months ago, in the course of a fortnight, he lost all the hair from his scalp, eyebrows, eyelids, nostrils and beard. There was marked associated formication. He had not previously noticed any thinning of his hair in the temporal regions, and he previously had a thick crop of grey hair.

On examination: He has a mild, but definite generalized ichthyosis. The palms and soles are normal. He presents the typical appearances of alopecia totalis, and in addition, on the sides of the scalp and face, and to a lesser extent the centre of the face, there is gross follicular plugging reminiscent of the appearances seen in chloracne.

Chest X-ray: Nothing abnormal noted. *Blood count:* Normal. *W.R.:* Negative. *Serum cholesterol:* 187 mg/100 ml.

Histology: (Biopsy: skin of L cheek). The section shows patchy hyperkeratosis, the granular layer being reduced to a thin line. Follicular plugging is a conspicuous feature, and there are many small deformed hair follicles, but they are not forming hairs. Sebaceous glands are large and numerous. A very slight chronic inflammatory reaction is present in the dermis.

Comment: Taken alone this man's striking follicular hyperkeratosis with plugging is unusual enough, but the association with alopecia totalis must be unique. Before either of these conditions occurred his skin had become ichthyotic, apparently as an aftermath of a generalized hypostatic eczema.

Has this man four independent skin conditions, or is there some relationship between them?

An ichthyotic skin might well be more prone to follicular hyperkeratosis, even late in life, or both conditions might result from some undiscovered metabolic disturbance. The hair loss is equally complete where the follicles are hyperkeratotic and where they are not.

When workers in a factory develop chloracne, the severity of the lesions is directly proportional to the amount of exposure to the fumes responsible, and no predisposition of certain types of skin has been recorded.

Dr I B Sneddon: I should have thought there was a possibility that this was a reticulosis. I have seen a similar follicular eruption as a pre-mycotic condition before, but this does not explain the alopecia.

Dr Louis Forman: Did he have contact with paraffin or mineral oil?

Dr R D Sweet: His job is dismantling unwanted naval wireless sets and other small items. I could not convince myself that his condition was anything to do with his work. Three other men who work with him were not affected. He had earlier used brilliantine on his hair when he had flowing white hair.

Dr M Garretts: I wondered whether this could be a case of ulerythema sycosiforme, but the fact that the hair loss preceded the appearance of the eruption makes this idea unlikely.

Dr B C Tate: Have any vitamin A studies been carried out on this man?

Dr R D Sweet: No.

Dr P R Montgomery: What about the exclusion of myxœdema in this case?

Dr J Savage: Before the discussion started I passed the time looking at Marshall's new book, and there is a picture in that of a similar facial condition due to the use of brilliantine.

REFERENCE
Marshall J (1960) Diseases of the Skin. Edinburgh and London

Professor J T Ingram: May I add to the confusion? The condition might be due to stress or shock. I recollect something like this in which there was also follicular plugging and inflammation.

Dr P J Hare: Mention of myxœdema recalls that there is a condition of 'thyroid alopecia' in dogs, particularly poodles, from which they get better when treated with massive doses of thyroid extract, although there is no evidence of thyroid deficiency. The histological picture in the canine disease resembles that of the patient shown today.

Dr Bentley Phillips: I should think lots of poodles are treated with brilliantine.

The following cases were also shown:

Borderline (dimorphous) Leprosy
Dr P J Hare & Dr W H Jopling
(1) **Kyrle's Disease**
(2) **Multiple Glomus Tumours**
Dr R J Cairns

Lymphatic Lymphoma
Dr M Garretts (for Dr P J Hare)
Poikiloderma Vasculare Atrophicans (Jacobi-Lane) with Reticulosis
Dr A W McKenzie (for Dr H J Wallace)
? Granuloma Annulare
Dr R H Champion (for Dr H J Wallace)
Pseudoxanthoma Elasticum with Arterial Calcification in a Young Female
Dr J Morgan
(1) **Rosacea (Lewandowsky)**
(2) **Dermato-fibro-sarcoma**
Dr I Martin-Scott
Keratosis Punctata
Dr K M Witham
(1) **Scleroderma with Atrophy**
(2) **Benign Forearm Poikiloderma**
Dr F Ray Bettley
Neurofibromatosis
Dr S Gold

Meeting December 15 1960

Cases

Diffuse Systemic Sclerosis

P F Borrie MD

N H, female, aged 54. Clerk.

History: Raynaud's phenomenon of the fingers began twenty years ago. Calcinosis cutis affecting the fingers and thumbs began four years ago as tender nodules which persist for three or four months and finally discharge a thick, creamy material. Complete or partial dispersion results, although a pitted scar may be left behind. Intermittent, severe, lower abdominal pain, accompanied by diarrhœa, began two and a half years ago. At the commencement it occurred for a day at a time once or twice a week. Two years ago it became severe and continuous with considerable melæna. She was admitted to hospital and transfused, a diagnosis of ulcerative colitis being made. Since that time there has been no further melæna and pain and diarrhœa have only recurred twice, for two months a year ago and for a week six months ago.

Family history: Negative.

Clinical findings: Acrocyanosis of fingers and hands. Hard nodules in pulps of left index finger and right thumb. Pitted scars in pulps of right thumb, right index finger and left fifth finger.

Investigations: Urine: nothing abnormal noted. Serum calcium: 10·8 mg/100 ml. Serum inorganic phosphate: 2·9 mg/100 ml. X-ray chest: nothing abnormal noted. X-ray fingers: large area of calcification in the tip of the left index finger with smaller calcifications in the left thumb and second and third right digits. There is also some absorption of the palmar aspects of the tufts of both thumbs, the right index and the left index and little fingers. Barium swallow, meal and enema – no functional or anatomical abnormality present, except for a wide-necked diverticulum in the ascending colon.

Comment: This case is presented as an example of diffuse systemic sclerosis on the evidence of the Raynaud's phenomenon and calcinosis cutis, the radiological evidence of absorption of the ventral surface of the terminal phalanges and the intestinal symptoms. The lack of both cutaneous sclerosis and radiological abnormalities in the gastrointestinal tract is not considered sufficiently important to vitiate this diagnosis.

Professor C D Calnan: I agree with the diagnosis. A great deal of special experience and skill may be required on the part of the radiologist in the investigation of these patients. One of the best methods for demonstrating the defect in function of the muscle of the gastro-intestinal tract is by contrast cine-radiography. In this way the immobility of the gut and pooling of barium can be observed almost better than by straight visual screening.

Dr F F Hellier: I think it is an important point that there may be disturbance of function before there are any anatomical changes which can be shown on simple X-ray. We had a patient in Leeds with minimal scleroderma in whom the X-ray of the chest was normal. She was seen by the chest physiologist in the thoracic unit and her respiratory exchange rate was markedly reduced. Thus there was gross functional abnormality before any evidence on X-ray. The same may apply to abdominal cases. Straight X-ray without special techniques will not show a functional bowel disturbance. This may be of wider application in scleroderma and functional tests may be needed before anatomical ones.

Dr G B Dowling: It is perhaps worth while having an œsophageal swallow examination done.

Dr P F Borrie: That has been done in the supine position and was negative.

Dr G B Dowling: That suggests the other abdominal symptoms were not genuine. The œsophagus is the most commonly disturbed before the mobility of the gut, &c. I think œsophageal peristalsis is disordered first, and abdominal changes follow later according to the literature. By the time you get diarrhœa it is pretty late.

Dr B C Tate: I am not happy about the diagnosis of scleroderma. I could find no signs of sclerosis of the face, mouth or fingers and I should have thought that these would have been apparent in true scleroderma, as the functional disturbance had been going on for twenty years.

Dr G B Dowling: Scleroderma of the fingers is not invariably present with Raynaud's symptoms and other manifestations of the 'systemic sclerosis' syndrome. One such patient had Raynaud's symptoms with absorption of terminal phalanges, calcinosis, a severe swallowing defect and the characteristic facies. The fingers were rather thick but perfectly mobile.

Dr S C Gold: If, as Dr Dowling says, sclerosis of the fingers or face are not necessary and it seems also that telangiectasia need not be present, then what are the minimal requirements for making such a diagnosis?

Dr H R Vickers: I agree with the diagnosis of systemic sclerosis. She has telangiectases on the face. I removed her face powder and counted five. In these difficult cases with few definite symptoms I feel that it is always worth while considering doing a renal biopsy, since if the kidney is involved, the diagnosis will then be established with certainty. I have had renal biopsies done in several of my patients and it is a procedure with very little risk which in this type of case is justifiable.

Pemphigoid with Malignant Melanoma

J M Marks MRCP (for S C Gold MD)

F T, female, aged 61. Housewife.

History: First seen in October 1956 on account of blisters in mouth which had been present for four months. Recent onset of sparse blisters on shoulder, face and scalp. Biopsy of blister showed histology consistent with a diagnosis of pemphigoid. Tzanck test for acantholytic cells negative.

November 1956: mentioned a mole on her back which had been present for years. This was originally flat, but for some time had been raised and for a year had been bleeding intermittently. It was excised and found to be a malignant melanoma.

Skin lesions settled without treatment, but buccal blisters continued.

December 1956: started on prednisone 10 mg/day. Maintained on a small dose of steroid with very little skin involvement, but with mouth lesions that fluctuated. In January 1960 blisters became much more troublesome and in May 1960 patient was admitted to hospital. On examination then there were blisters in the mouth and blisters and gyrate erythema of the trunk and limbs (Fig 1). In the right axilla was an enlarged lymph node,

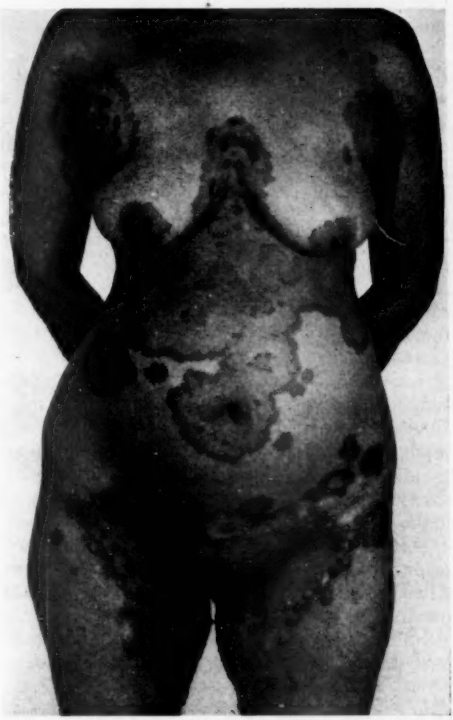

Fig 1 *Pemphigoid with malignant melanoma, May 31, 1960*

said to have been present for two months. Treatment with prednisone, adrenocorticotrophic hormone (ACTH) and sulphapyridine produced improvement of the skin and mucosæ. The patient was about to be discharged when she developed a

temperature of 101°F and further enlargement and tenderness of the lymph node in the axilla. There was no skin sepsis and no abnormality in other systems. Chest X-ray was then normal.

Temperature returned to normal and lymph node became smaller and less tender after a course of penicillin. Lymph node excised October 1960. Histology showed deposits from melanoma. Maintained with clear skin on 5–10 mg prednisone/day.

November 1960 admitted for excision of skin nodule. Hæmoptysis while in hospital.

Clinical findings: Scars of lymph node and skin nodules. No blisters on skin or in mouth.

Investigations: Chest X-ray taken 1.11.60 after hæmoptysis showed widespread metastases throughout both lung fields.

Comment: This patient with pemphigoid presented with blisters in her mouth. Minor skin involvement appeared within four months of the onset of the disease but serious skin lesions did not occur until much later, the major episode starting in January 1960. Because of the predominance of mouth blisters and sparse, fixed skin lesions a diagnosis of benign mucous membrane pemphigus was considered, but the eyes and other mucous membranes never showed signs of disease. A malignant melanoma was excised within a few months of the onset of the illness. For three years after the blisters were controlled by relatively small doses of prednisone (5–20 mg/day). In January 1960 the dose had to be increased until June 1960 when the patient was taking 60 mg prednisone/day as well as ACTH and sulphapyridine. While on her maximum dose of prednisone, she developed a large, tender lymph node in the right axilla.

Histological examination showed necrosis and secondary deposits from the malignant melanoma. After excision of the lymph node it became possible to keep the blisters under control on 2·5–5 mg prednisone/day. Secondary deposits have since developed in the lungs and skin.

Dr S C Gold: It took me some time before I realized that the pemphigoid could be related to the development of malignant melanoma but in retrospect the timing does coincide well. What the febrile upset which occurred with increased swelling and tenderness of the axillary gland could have been due to is most uncertain. The section from this gland shows extensive necrosis in the secondary deposit and one wonders if the high dosage of steroids being given at that time could be connected with this inflammatory process.

Dr F F Hellier: In a recent article, Cooke (1960) has suggested that one can distinguish pemphigus from pemphigoid because the latter affects chiefly the palate and gums, whilst pemphigus occurs more marked on the red borders of the lips and the mucus membrane of the cheeks. Do members agree with this?

REFERENCE

Cooke B E D (1960) *Brit. Dent. J.* **109**, 131

Dr S C Gold: I have seen two other patients with pemphigoid occurring with carcinoma of the bronchus. Both had severe buccal involvement and I wonder if such an association is common in those related to cancer.

Dr H T H Wilson: I had a similar case, a lady with an inoperable carcinoma of the breast and pemphigoid. She had several lesions in the mouth which bled freely. It is certainly well worth considering the possibility that lesions in the mouth are more common in cases associated with carcinoma.

The following cases were also shown:

Urticaria Pigmentosa
Dr R M B McKenna

(1) **Keratosis Pilaris with Cicatricial Alopecia and Bilateral Congenital Cataract**
(2) **Acne Conglobata**
Dr P F Borrie

A Case for Diagnosis? Sub-corneal Pustular Dermatosis? Psoriasis
Dr M Smith

(1) **Reticulosis**
(2) **Dermatitis Herpetiformis**
Dr A Scott

Scleredema Adultorum (Buschke)
Dr Harold Wilson

Lichen Planus Atrophicus; Pseudo-pelade
Dr C M Ridley (for Dr Brian Russell)

Clinical Section

President T C Hunt DM

Meeting November 11 1960

Cases

Carotid Body Tumour Associated with Diarrhœa and Abdominal Pain

Zoë D Chamberlain MB (for T C Hunt DM)

Mr F C, aged 54

History: 1944: A small mass was noted in the right side of the neck. It was excised and, as it was thought to be a secondary deposit of carcinoma, the area of excision was irradiated.

1951: The mass recurred and gradually increased in size. Biopsy showed the appearances of a carotid body tumour.

1956: The patient began to experience severe cramping abdominal pain and bouts of diarrhœa (7–8 loose motions daily, without blood or mucus). Investigation elsewhere suggested steatorrhœa and he was put on a gluten-free diet without effect.

1958: Reinvestigation suggested intestinal hurry rather than steatorrhœa.

1960: Admitted to St Mary's Hospital (Dr T C Hunt). Symptoms unchanged. During the previous four years had received opiates, chlorpromazine and ganglion-blocking drugs without effect.

On examination: Florid complexion. Firm swelling on the right side of the neck, irregular, tender, approximately 5 × 4 in. (Fig 1). BP 110/70. Pulse 70 regular. Heart normal. Chest clear. Tendon reflexes absent, C.N.S. otherwise normal. Slight tenderness in the epigastrium and left hypochondrium. Liver palpable 1½ in. below right costal margin. Sigmoidoscopy normal on several occasions.

Investigations: X-rays: Barium meals: January 1958, normal. November 1958, barium reached the colon in 20 mins and the rectum in one and a half hours; normal colonic mucosa. August 1960, barium reached the rectum in one and a half hours; otherwise normal.

Chest: normal. Cervical spine: narrowing of C.V. 6/7 disc space.

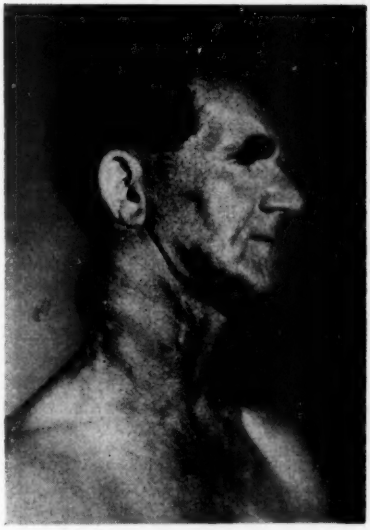

Fig 1 *Photograph showing tumour before excision*

Skull: no evidence of bone erosion.

Urine: 5 hydroxy indole acetic acid output normal. No catechol amines.

Stools: No intestinal pathogens. Fæcal fats 2·4 g/three days. (80 g fat/day diet.)

Liver function tests: S.G.O.T. 35, S.G.P.T. 50 units/ml. Total bilirubin 0·7 mg/100 ml. Alkaline phosphatase 4·1 K.A. units/100 ml. Thymol flocculation negative.

Serum protein: Total 6·9, albumin 4·2, globulin 2·7 g/100 ml.

Glucose tolerance test normal.

Serum calcium 9·3 mg/100 ml. Plasma electrolytes and blood urea normal.

Hb 13·6 g/100 ml. W.B.C. 7,000 (normal differential count). E.S.R. 5 mm in one hour (Wintrobe).

ECG normal.

Operation: The mass was removed in two stages – the first was performed by Professor C G Rob (under hypothermia) on 29.8.60 and the second by Mr J Fairgrieve on 13.10.60. The locally extensive tumour was excised without ligation or grafting of the carotid vessels and without the patient developing a hemiplegia as has so often followed operations of this type.

Histology: On microscopy the mass was shown to be a carotid body tumour of the type resembling the normal carotid body. The chief cells were polygonal (with large volumes of pale staining, finely granular cytoplasm and hyperchromatic nuclei), divided into clusters by fibrous vascular stroma. It is unusual for carotid body tumours to metastasize to lymph nodes but one section of the mass showed such a node with lymphatic and tumour tissue within the capsule.

Comment: The mass caused minimal local disturbance to the patient despite its size and slight tenderness, but the diarrhœa and abdominal pain have caused him great distress. His symptoms of diarrhœa and pain have improved very considerably post-operatively; he now has an average of 2 motions a day instead of the previous 7 or 8. This case was shown as we suggest that there may be a relationship between the tumour (first noted in 1944) and the severe diarrhœa with intestinal hurry (first occurring in 1956). It seems possible that the secretion of some substance by the carotid body tumour affected the gut and caused the symptoms although, as yet, this substance has not been identified.

Lead Encephalopathy

A K Thould MD MRCP (for M G Ashby MRCP)

Lead encephalopathy is now very rare but occasional examples are still found in emergency admissions to general medical wards.

History: Mrs W, aged 46, had been employed in a lead accumulator factory for the five years before this admission in April 1960, during most of which time she had supervised the spreading by machine of a moist mixture of litharge and red lead on to lead accumulator plates. She was inadequately protected from fumes and her environment was very dusty. She had been in good health previously, and had had one live child now aged 14, and one miscarriage at twelve weeks four years before becoming exposed to lead.

In September 1959, glycosuria was found and a glucose tolerance test gave a mildly diabetic type of curve. She was treated by weight reduction and was in good health until January 1960 when she developed frontal headaches when tired. In March 1960 two generalized epileptiform convulsions occurred followed by transient diplopia and forgetfulness. She had one further epileptiform convulsion and, two weeks before admission on 29.4.60, she became delirious. After treatment she remembered that she had had some colicky abdominal pain for two or three months.

She was admitted to the Whittington Hospital with a provisional diagnosis of an intra-cranial space-occupying lesion.

On examination: moderately obese, slow in speech and thought, lethargic. Marked bilateral papilloedema and three-flame-shaped hæmorrhages visible in the left fundus. She had an obvious lead line round the base of the teeth, but not at the anus. Heart clinically normal, BP 105/65. (The blood pressure was normal throughout), pulse 110, afebrile. No evidence of muscular weakness; all reflexes present, though sluggish. Conjunctivæ pale.

Investigations: Hb 75% Haldane, R.B.C. 4,165,000. P.C.V. 35%, M.C.V. 84 cu.μ M.C.H.C. 30%. Basophilic stippling was present in approximately 3,700 red cells per million counted. E.S.R. 32 mm in the first hour (Westergren), W.B.C. 10,700 (polys. 68%, lymphos. 30%). The red blood cells appeared hypochromic. C.S.F. clear, protein 45 mg%, white cell count 10/c.mm, sugar 75 mg%, this specimen being obtained from the ventricles. Coproporphyrin III was present in excess in the urine, and a twenty-four-hour specimen of urine contained 400 μg of lead (normal for this laboratory 30–80 μg). Blood urea 18 mg/100 ml, a glucose tolerance test showed a normal curve, no glycosuria. Total urinary creatinine 960 mg/24 hours, creatine nil. S.G.O.T. 26 units ml.

A ventriculogram was normal (Mr I R McCaul) and a diagnosis of lead poisoning with lead encephalopathy was made.

Treatment: Calcium di-sodium versenate, 3g in 50 ml of normal saline, was given by intravenous injection, over 5–10 minutes, once daily for five days, as recommended by Sidbury (1955). Urine was collected for the first and last twenty-four hours of this course and the lead content estimated. Only a small quantity of lead was found in

the urine. A second course was therefore instituted five days later, giving 2 g in 500 ml normal saline, intravenously over a period of two to three hours, once daily for five days, as recommended by Leckie & Tompsett (1958). Her twenty-four-hour urinary excretion of lead on this regime was 3·63 mg on the first day, 2·65 mg on the second and 1·80 mg on the fifth. She became much brighter after this treatment and lost her headaches, and was finally discharged well on 2.6.60.

Follow-up: 17.6.60: She looked a different woman, healthy, and much more alert physically and mentally. Her papillœdema had disappeared. Hb 106%. No punctate basophilia seen.

Discussion: With modern exhaust-ventilation techniques and sensible and thorough care of the workers in factories using lead, lead poisoning and particularly lead encephalopathy has become a rarity. Lead encephalopathy may present with epileptiform convulsions, coma, delirium, transient paresis, aphasia and headache, and chronic cases may show mental dullness, poor concentration and memory, trembling and deafness.

Calcium di-sodium versenate forms a very stable complex with lead, and does not cause tetany in man (Spencer *et al.* 1952). It is best given by intravenous injection, being only poorly absorbed by mouth (Sidbury 1953). It is most effective when given over a period of three to six hours and increasing the daily dose above 2 g causes no appreciably greater increase in lead excretion (Leckie & Tompsett 1958). We found here that a rapid once-daily injection was unsatisfactory, and more prolonged administration was necessary. Sodium versenate has been known to cause acute renal tubular necrosis in man, though not the calcium di-sodium salt (*Lancet* 1955, Dudley *et al.* 1955).

It must be emphasized that though the presence of punctate basophilia and urinary coproporphyrin III in significant amounts implies increased lead absorption, it does not necessarily imply lead poisoning (*see* Table I), as the patient may not be susceptible (Hunter 1959): the presence of specific symptoms and signs is also necessary. Symptoms suggestive of an intracranial lesion, together with evidence of increased lead absorption, *may* mean lead poisoning with encephalopathy, but may be a coincidental association. The diagnosis of lead encephalopathy, in view of its great rarity now in this country, should be made with caution.

Table I

Date	*Hæmoglobin (% Haldane)*	*Urinary coproporphyrin III*	*Reticulocyte %*	*Punctate basophilia per million RBC*
13.1.59	91	+	3·2	375
29.9.59	98	+	1·4	2,400
15.3.60	70	++	9·0	3,400
24.4.60				3,000
27.4.60	75	++		3,700
12.5.60	76		1·0	< 500
18.5.60	81		1·5	< 500

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Hunter D (1959) Health in Industry. p 113. Harmondsworth
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Leckie W J H & Tompsett S L (1958) *Quart. J. Med.* **27**, 65
Sidbury J B Jnr
(1953) *Proc. Soc. exp. Biol. N.Y.* **82**, 226
(1955) *Amer. J. Med.* **18**, 932
Spencer H, Vankinscott V, Levin I & Laszlo D (1952) *J. clin. Invest.* **31**, 1023

Budd-Chiari Syndrome

A B Miller MB (for T Parkinson MD FRCP)

Mrs T W, aged 22, housewife. First admitted 29.12.59.

The patient is a young woman who suddenly developed severe ascites. Inoperable malignant disease was diagnosed but at laparotomy gross hepatomegaly and splenomegaly with a raised portal venous pressure suggested a diagnosis of the Budd-Chiari syndrome, and this was confirmed by liver biopsy. Polycythæmia rubra vera proved to be the underlying cause. The importance of this case lies in the dramatic response by an apparently dying woman to treatment with anticoagulants and pyrimethamine.

History: nine days' malaise and nausea (beginning the day after a party). Eight days' swelling of abdomen and loose motions. Seven days–eyes appeared yellow, urine dark and motions grey. From then until she was admitted progressive abdominal enlargement occurred. At no time did she have abdominal pain, apart from a feeling of tightness.

On examination: Cachectic, not clinically jaundiced. Gross ascites and a large epigastric mass. After paracentesis of 22 pints of clear yellow fluid, it became apparent that the abdominal mass was a large liver. A provisional diagnosis of secondary neoplasia was made.

Investigations: Hb 98%. W.B.C. 19,000 (neutros. 80%, lymphos. 14%, monos. 4%, eosinos. 2%). E.S.R. 1 mm in the first hour. S.G.O.T. 36 units. Van den Bergh: direct, weak biphasic; indirect, 2 mg%. Alkaline phosphatase 30 K.A. units. Thy-

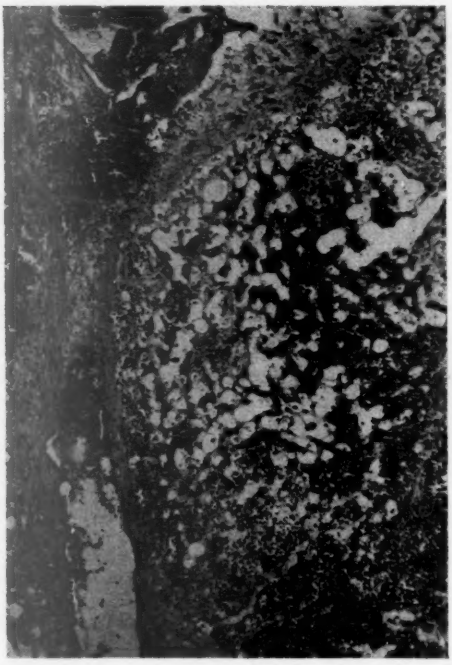

Fig 1 *Thrombosis in a hepatic vein : centrilobular necroses and sinusoidal congestion*

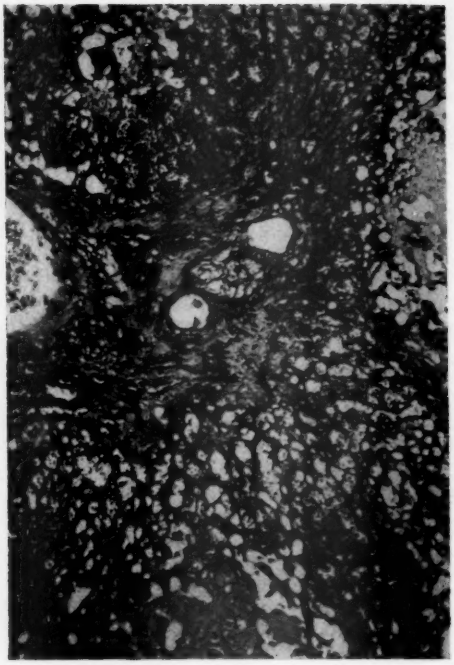

Fig 2 *Recanalizing thrombus*

mol turbidity 2 units. Zinc sulphate 6 units. Chest X-ray normal. X-ray abdomen – large soft-tissue mass seen in left hypochondrium. Ascitic fluid – few cells (R.B.Cs., lymphocytes, endothelial cells, no malignant cells seen).

Laparotomy 12.1.60 (Mr D Harland): Gross hepatomegaly and splenomegaly (approximately 25 cm in diameter). Portal venous pressure 300 mm water. Liver biopsy taken.

Liver biopsy: Thrombosis in some of the larger hepatic veins. Intense dilatation and congestion of the sinusoids with centrilobular necrosis. Liver pattern retained. No cellular infiltration or biliary retention (Figs 1 and 2).

Subsequent investigations: Hb 106%. R.B.C. 6,080,000. W.B.C. 22,100. Platelets 576,000 per c.mm. P.C.V. 59%. Bone-marrow smear normal. Hæmoconcentration was not thought a likely explanation of these findings in view of persistently raised results, and polycythæmia rubra vera was diagnosed.

Progress: In view of the severity of her illness it was decided to start treatment with anticoagulants. Phenindione was given in sufficient dosage to keep the prothrombin time at two to three times the control. Initially only 10 mg daily was required, but as the patient's clinical state improved the amount of phenindione had to be increased until a daily dose of 50 mg was reached after three months. Requirements have since been stable. The ascites was treated by hydroflumethiazide 200 mg daily five days per week, together with mersalyl 2 c.c twice weekly. Paracentesis at approximately fortnightly intervals was required for two months but has not been required since 9.3.60. Pyrimethamine 25 mg daily was given from 30.1.60 for the polycythæmia (*see* Fig 3).

18.2.60: Barium swallow showed no œsophageal varices.

11.3.60: An attempt was made to demonstrate the inferior vena cava radiologically by a venogram via the femoral route. It was hoped to exclude stenosis of the inferior vena cava (there has never been any clinical evidence of this). Unfortunately, the catheter penetrated the wall of the inferior vena cava and the dye extravasated.

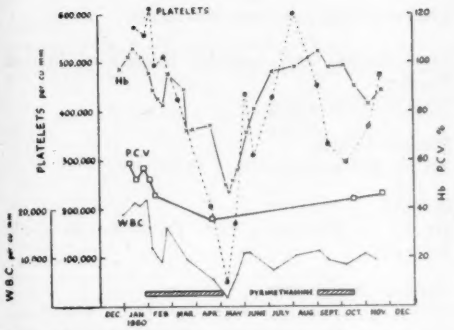

Fig 3 *Chart showing response of polycythæmia to pyrimethamine 25 mg daily*

Following this procedure the patient's condition was satisfactory and she was discharged home on 13.3.60.

16.3.60: Readmitted with hæmorrhage from the wound in the left groin through which the cavagram was attempted. The bleeding ceased after extensive diathermy though a 2-pint blood transfusion was required. The wound was slow to heal but eventually she was discharged on 13.4.60.

22.4.60: Hb 75%, W.B.C. 5,300, P.C.V. 36%, platelets 203,000. Pyrimethamine was stopped on 6.5.60 and as the ascites was controlled mersalyl was also stopped.

14.5.60: Readmitted because of rapidly progressing pallor and bruising. Hb 46%, W.B.C. 1,600 (neutros. 70%, lymphos. 26%, monos. 4%), platelets 41,000 per c.mm. Liver function tests: Serum bilirubin 1·5 mg%, S.G.O.T. 22 units, alkaline phosphatase 38·2 K.A. units, thymol turbidity 1 unit, zinc sulphate 5 units. Following a 2-pint blood transfusion she gradually improved. A repeat barium swallow showed no evidence of œsophageal or gastric varices.

She was allowed home on 25.5.60 and has since been treated as an outpatient on long-term anticoagulant therapy.

2.9.60: Ascites no longer detectable; hydroflumethiazide reduced to 200 mg twice weekly. Hb 105%, W.B.C. 11,700, platelets 602,000 per c.mm. Pyrimethamine 25 mg daily was again given till 20.10.60, when Hb was 91%, W.B.C. 8,200 and platelets 297,000. Liver function tests (14.10.60): Serum bilirubin 1·0 mg%. S.G.O.T. 20 units, alkaline phosphatase 20·2 K.A. units, thymol turbidity 5 units, zinc sulphate 10 units. 28.10.60: Barium swallow showed no œsophageal varices.

November 1960: The patient feels extremely well. She has been working (as a secretary) full time for two months. Examination reveals no ascites or œdema. The liver is palpable 3 cm and the spleen 5 cm below the costal margin.

Discussion: The Budd-Chiari syndrome is a condition characterized by occlusion of the hepatic veins by thrombi with resultant hepatomegaly from intense centrilobular sinusoidal congestion. The development of the condition is usually rapid with upper abdominal pain, ascites, portal hypertension, liver failure and death. Gibson (1960) distinguishes Chiari's disease from the Budd-Chiari syndrome, the primary lesion in Chiari's disease being occlusion of the ostia of the hepatic veins.

The Budd-Chiari syndrome is allied to the condition of veno-occlusive disease of the liver found in Jamaica. Stuart & Bras (1957) attribute this to poisoning by 'bush teas' made from senecio and *Crotalaria retusa* plants. The characteristic histological picture is thrombosis of the smaller hepatic veins with sparing of the larger hepatic veins, the opposite to that usually described in the Budd-Chiari syndrome.

The ætiology in cases of the Budd-Chiari syndrome is often obscure though Palmer (1954) lists many causes. Polycythæmia rubra vera is a well-recognized cause, though most authors point out the difficulty in distinguishing this from hæmoconcentration in the acute phase. Fitzgerald *et al.* (1956) report a young woman whose polycythæmia responded to treatment with radioactive phosphorus. Parker (1959) in a review of the literature, mentions 14 cases in which polycythæmia was suspected. In the present case the very high platelet count and raised white cell count were felt to confirm the diagnosis of true polycythæmia; Blood volume studies were not possible. Pyrimethamine (Daraprim) is an antimalarial drug with a weak anti-folic acid action. Isaacs (1954) found it of value in the treatment of polycythæmia rubra vera even in patients resistant to radioactive phosphorus. An annotation in the *British Medical Journal* (1956) mentions the possibility of a rapid fall in red cells and this was seen in this patient as part of a fall in all elements of the bone-marrow (*see* Fig 3).

It seems rational to treat a disease characterized by progressive venous thrombosis with anticoagulants. Norris (1956) reports a case where anticoagulants were used. Treatment was begun with phenindione 100 mg twice daily, but within twenty-four hours the prothrombin time rose to 75 seconds and anticoagulants were stopped. Norris feels anticoagulant therapy is hazardous. In the present case the pre-treatment prothrombin time was 18 seconds (control 12 seconds) and therefore treatment was begun with very small doses of phenindione, though the dose had gradually to be increased as the patient's clinical state

improved. Coincidentally the necessity for paracentesis ceased and the requirements of diuretics diminished.

The prognosis in this case is uncertain. It seems likely that cirrhosis will develop following the gross destruction of liver cells in the biopsy. Nevertheless, reticular stains showed that the architecture of the liver was undisturbed and the capacity of the liver to recover from gross destruction is well recognized. The liver function tests are still abnormal, but the absence of œsophageal varices is an encouraging feature.

ADDENDUM: March 1961: Patient remains well on long term anticoagulant therapy.

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The following cases were also shown:

Myelomatosis and Anæmia: Results of Steroid Therapy
Dr R R de Mowbray

Duodenal Polyp
Mr I D B Rennie (for Mr F N Glover)

Œdema
Dr C N Mallinson (for Professor W J H Butterfield)

Chronic Cholecystitis
Mr A E Wheatley (for Mr H E Lockhart-Mummery and Dr R S Bruce Pearson).

Posterior Exenteration
Mr J M Brudenell (for Mr G E Parker and Mr C K Vartan).

Epidermolysis Bullosa
D M Danks MD MRACP (for E J Moynahan MD FRCP).

Meeting December 9 1960

Cases

Acute Non-specific Pericarditis Associated with High Titres to a Coxsackie Group B_4 Virus

A J Lane MB BChir (for R J Harrison MRCP)

The condition of non-specific pericarditis (so-called idiopathic or benign) has been well known for many decades. Most authors writing recently on it regard it as a syndrome of varied ætiology. It has been reported following trauma, and serum injections, and in association with mumps, infectious mononucleosis, atypical pneumonia, upper respiratory infection. In particular the association with epidemic pleurodynia has been repeatedly noted (Bing 1933, Aagaard & Jensen 1952).

Recently Coxsackie group B viruses have been shown to be constantly associated with epidemic pleurodynia, as well as with cases of infantile myocarditis and a proportion, perhaps a fifth, of aseptic meningitis cases. However, only in the past three years has the association with non-specific pericarditis been reported. There appear to be 21 cases in the American literature (*see* Table 1) but only 2 cases have been reported from this country, both from Northern Ireland (Fletcher & Brennan 1957, 1958). In only 2 cases was the virus cultured from pericardial fluid, thus fulfilling Kilbourne's (1952) criteria that to establish a diagnosis of virus infection an adequate antibody response to a grown virus should coincide with the patient's illness, that the virus should be recovered from the pathological specimen, and that there should be no other known pathogen related to the patient's disease. Of the other 21 cases there was an antibody response in 9. This was associated with positive stool cultures in 5 but in view of the existence of symptomless excreters the significance of this is uncertain. In no less than 12 of the reported cases the evidence rested on convalescent titres only, some of which appear to be rather on the low side.

In the present case a high and rising titre to Coxsackie group B_4 viruses coincided with clinical and electrocardiographic evidence of pericarditis.

Case Report

P B, male, aged 25. Hospital electrician.

Presented on 2.5.60, complaining of dull aching lower substernal pain which had come on suddenly eighteen hours previously. It had subsided overnight but recurred that morning when he exerted himself at his work. The pain was made worse by sudden or violent trunk movements. He had felt shivery and hot and cold at the time of the onset. Three months previously he had been treated for acute superficial keratitis, presumably viral, which had completely subsided after a few weeks.

Table 1
Cases of Pericarditis with Coxsackie Group B Virus

Author	*Cultured from pericardial fluid*	*Changing antibody titre with stool culture:* (a) *Positive*	(b) *Negative*	*Convalescent titre raised*
Weinstein 1957				1
Fletcher & Brennan 1957			1	
Fletcher & Brennan 1958				1
Kagan & Bernkopf 1957	1			
Movitt *et al.* 1958			1	
McClean *et al.* 1958				4
Gorden *et al.* 1959		1	1	5
Gillett 1959		2		
Null & Castle 1959			1	1
Roberts *et al.* 1959		1		
Bell & Mies 1959		1		
Brodie & Marchessault 1960	1			
Present case 1960			1	
Totals	2	5	5	12

On examination: Marked tachycardia occurred on the slightest exertion. There was no pericardial rub, he was apyrexial and there were no other abnormal physical signs.

Investigations: ECG: forty-eight hours after the onset of pain there were raised saddle-shaped S–T intervals in leads II, III, AVF and V4, 5 and 6. The T wave was inverted in lead AVL. Four days later changes were more pronounced. After three weeks the ECG had reverted to normal.

Virus studies: Serum taken on the third day of illness showed a titre of 1/640 on the neutralization test with Coxsackie group B_4 virus. Ten days later the titre had risen to 1/1,280 and six days later it had fallen to 1/640 again. Tests against group B_1, B_2, B_3 and B_5 were negative at 1/300. Chest X-ray normal. Hæmoglobin, white cell count, sedimentation rate all normal.

Treatment: Entirely conservative. With bed rest the pain subsided within a few hours and did not recur.

Comment: The symptoms of acute non-specific pericarditis, range from very mild chest pain, to one mimicking infarction, and the duration from a day or two to recurrent attacks over seventeen years. The outcome may be benign, or fatal from cardiac tamponade. Although no rub was heard in our case, this has been a common experience – in up to one-third of cases from the longer series. The accepted minimum criteria appear to be characteristic pain with either a rub or ECG changes of pericarditis, for which no specific cause can be found. In our case there was no evidence of rheumatism or ischæmic heart disease, and the benign course would appear to rule out other diagnoses.

A virus ætiology was suggested to us because the present case occurred at the end of a period of six months in which there were 11 similar cases in St James Hospital, Balham (out of a total of 15 in two years). Virus studies were made in 4 other cases. In 2 they were negative and in 2 falling titres to Coxsackie group B_1 (1/256 to 1/64) or B_2 (1/32 to 1/16) were found. These results were interpreted as only suggestive of recent infection. During the same time there were several admissions for pleurodynia and aseptic meningitis but no evidence of Coxsackie infection was found.

In assessing the significance of a raised antibody titre it is necessary to know the incidence in the general population. Cook, who carried out the immunological tests in this case, found in 1958 that up to 60% of symptomless adults in this country showed raised titres of neutralizing antibody to Coxsackie group B virus (Cook & Smith 1960). In no case did the titre exceed 1 : 300. The titre of 1 : 1,280 in this case is regarded as strong evidence of recent infection, though only a two-fold rise was observed. Our patient had had no other recent illness except a keratitis, and this has no known association with the Coxsackie viruses.

In conclusion this case is presented as a possible but unproven case of Coxsackie pericarditis. Only more widespread investigation can establish the importance of the Coxsackie viruses in pericarditis as seen in this country.

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Weinstein S B (1957) *New Engl. J. Med.* **257**, 265

A Transient Syndrome with Peutz-Jeghers Features and Ectodermal Change

J A Kennedy MB DMRD and Cedric Hirson MRCP

Female, aged 69

Until six weeks before admission, active and well without relevant personal or family history. Sudden onset of anorexia, nausea and loss of taste followed two weeks later by explosive watery morning diarrhœa without blood or mucus; no pain. Partial response to constipating mixtures. After further two weeks almost all her hair fell out and the nails degenerated from the bases. She noted the development of pigmentation particularly on the hands. There was 1 stone loss in weight and marked constitutional disturbance.

On admission: The face and hands showed widespread general pigmentation. There were pigment spots about 2–3 mm in diameter on the hands and perineum. No buccal pigmentation. Almost total alopœcia. Nails dark and detaching proximally. Central depapillation of the tongue. Afebrile. No anæmia, clubbing or palpable lymph nodes. Breasts, thyroid, heart, lungs, blood pressure, abdomen, rectal examination, central nervous system all normal. Sigmoidoscopy: flattish nodular excrescences on the bowel wall were seen above about 10 cm; slight hyperæmia but no bleeding or ulceration.

Investigations: X-rays: Chest normal. Œsophagus – a few small polyps. Stomach and large intestine – widespread fine cobblestone appearances compatible with multiple adenomatous polyps (Figs 1 and 2). Small intestine – a few small polyps. These changes were confirmed by repeat examination. Blood count, serum proteins, electrolytes, urea, liver function tests, prothrombin time, E.S.R., ECG and urine all normal. Stools repeatedly normal; no ova, parasites or pathogens; trypsin present. Diagnex test and histamine test meal – achlorhydria. Agglutinations against salmonella and brucella negative. Histoplasmin skin sensitivity negative. Nail for heavy metals – no arsenic. Pyruvate tolerance and five-day fat balance normal. Glucose tolerance: 100, 210, 125 mg/100 ml.

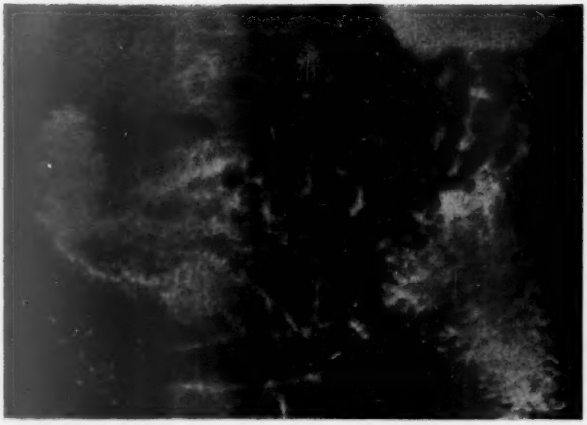

Fig 1 *Barium meal showing gastric polyposis*

Fig 2 *Barium enema. Post evacuation film showing multiple small polyps*

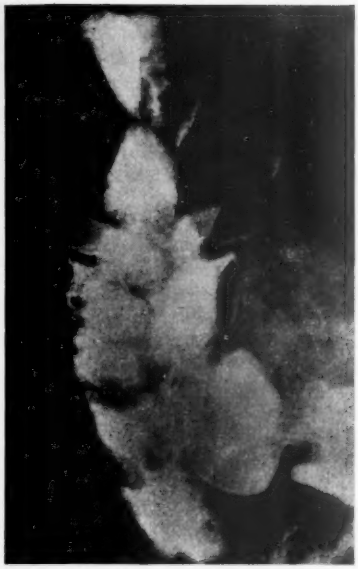

Fig 3 *Barium enema showing almost complete disappearance of polyps*

Soon after admission and without specific therapy, the symptoms subsided but she subsequently developed a chest infection which resolved completely. One month after admission sigmoidoscopy showed only some mild granularity of the mucosa and subsequent repeat X-rays showed almost complete resolution (Fig 3).

Pigmentation faded, hair and nails regrew normally over the next four months and, at the time of presentation, the patient was free of abnormal physical findings.

Discussion: Initially, in view of the radiological and sigmoidoscopic appearances together with the macular pigmentation, Peutz-Jeughers syndrome was considered but the history, clinical picture and subsequent progress were not consistent with this. No biopsy of the gastro-intestinal lesions was performed but it is considered that these must have been of the nature of mucosal pseudo-polyps. A comparable clinical picture of gastro-intestinal and ectodermal change was reported by Cronkhite and Canada (1955) but their two cases exhibited severe malabsorption and ended fatally. The progress of the illness in this case suggests a temporary infective or toxic cause.

REFERENCE
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Carcinoma of Œsophagus

J W Bradbeer FRCS (for Norman C Tanner MD FRCS)

E M R, female, aged 70
First attended St James' Hospital in 1949 with a three-month history of progressive dysphagia.

Investigations: Barium swallow showed an œsophageal filling defect just below the aortic arch. The raised edge of a tumour was seen at 27 cm from the incisor teeth on œsophagoscopy.

Operation (1.12.49): Left thoracotomy. The growth, found immediately below the arch of the aorta, was adherent on all sides and was freed with difficulty. The lower two-thirds of the gullet was removed after transecting the cardia and dividing the œsophagus above the aortic arch. The paracardiac and left gastric glands were removed with as many mediastinal glands as possible. After mobilizing the stomach an end-to-end œsophagogastrostomy was carried out.

Specimen: A malignant ulcer was found 2½ in. in length completely encircling the œsophagus. Histological examination revealed a well differentiated squamous cell carcinoma which had infiltrated to the superficial layer of muscle.

Progress
April, 1952: The patient noticed a lump on the front of the right thigh – this was excised at another hospital. Histological examination showed a squamous cell carcinoma. In September the patient's attention was drawn to a further lump in the same site.

On examination (20.10.52): A 5-in. healed scar on the front of the right thigh. A long lobular mass was felt deep to the scar with two further nodules, one proximal and one distal to it.

Operation (9.9.53): Wide local excision of the extensor muscles of the thigh sacrificing the femoral nerve.

Histology: Invasion of muscle by squamous cell carcinoma.

March, 1954: Pain drew the patient's attention to a further lump above the right groin. Examination revealed a firm mass, 4 cm in diameter, above the inguinal ligament fixed to the lateral pelvic wall.

Operation (18.3.54): A cystic mass was found adherent to the external iliac vessels, round ligament and peritoneum. A block dissection was carried out removing the mass, the inguinal ligament, muscle, fascia and glands down to the external iliac artery. Section of a gland showed metastasizing squamous cell carcinoma. A course of post-operative deep X-ray therapy followed.

Present condition: The patient can swallow normally. She has no heartburn. There is no evidence of regional or distant metastases.

Comment: This patient is presented for two reasons. Firstly, it is sometimes stated that the tumour in those patients who survive for long periods after cancer surgery differs from the usual type. On this occasion, however, the squamous cell carcinoma behaved in the same way as any other malignant tumour, metastasizing via the blood stream and the lymphatics. Hæmatogenous spread to the thigh muscles occurred three years, and lymphatic spread to the iliac glands five years, after the original operation.

Secondly, this patient remains well eleven years after œsophagectomy and six years after removal of secondary deposits.

Carcinomatous Neuropathy with Papillœdema

[*Abridged*]

P D B Davies MD MRCP

A man aged 56 was well until 8.5.60 when he injured his chest at work. A month later he presented with a large left hæmothorax and several rib fractures.

Chest X-ray showed, in addition to the pleural effusion, an opacity in the left upper lobe. One specimen of sputum contained epithelial cells very suggestive of malignancy. In life, no other evidence of cancer was found. Repeated examinations of sputum revealed no more malignant cells; bronchoscopy showed no tumour though there was some compression of the left bronchial tree (attributed to the pleural effusion) and the segmental orifices of the left upper lobe could not be seen; all specimens of fluid aspirated from the hæmothorax were examined for malignant cells but none was found; there was no sign of cancer in two pleural biopsies. After his death on 18.9.60 we saw an oat cell carcinoma of the apico-posterior segmental bronchus of the left upper lobe with a solitary metastasis in a lymph gland at the hilum.

Shortly after admission to the Whittington Hospital on 13.6.60 he began to complain of paræsthesiæ in the hands and feet and of pain felt in the proximal muscles of the limbs. Then he noticed weakness and clumsiness of the limbs and we noticed mental changes with confusion and euphoria. The neuropathy progressed rapidly with increasing loss of power and muscle wasting with loss of limb reflexes. At the same time all forms of sensation were increasingly blunted. There were no cranial nerve, pyramidal or cerebellar signs.

A month after admission, though he made no complaint of loss of vision, papillœdema, which had not been present on admission, was found; the changes were well marked but there were no hæmorrhages or exudates. At the time the papillœdema was assumed to be a sign of raised intracranial pressure caused by secondaries and so no further investigations were made. It was observed, however, that there were no other symptoms or signs of increased intracranial tension such as headache or vomiting and that there were no signs of focal lesions in the brain.

At the post-mortem not only were no intracranial secondaries found but there was no sign of raised intracranial pressure. The optic nerves were taken for histological examination. They showed degeneration, gliosis and round cell infiltration. It seems likely therefore that the papillœdema was due to optic neuritis. This possibility will be discussed more fully elsewhere.

There is no reference in the literature to an association of papillœdema with cancer but if real then it may be important. Our patient had what we now know was an operable growth but operation was not considered because of the mistaken assumption of secondaries.

REFERENCE

Brain R & Henson R A (1958) *Lancet* ii, 971

Dr F Clifford Rose (London) said he had recently reviewed 20 cases of carcinomatous neuromyopathies admitted to the National Hospital, Queen Square. One of these cases was very similar to the case shown by Dr Davies. He was a man aged 48, and was under the care of Dr S P Meadows. He presented with blurred vision and 'pins and needles' in his hands and feet. Examination revealed bilateral papillitis which later went on to consecutive optic atrophy with diminished visual acuity. He also had a typical asymmetrical peripheral neuropathy. The C.S.F. revealed a protein of 130 mg%, 13 lymphos./c.mm and a mid-zone Lange curve. Although X-ray of the chest was normal, at post-mortem an oat-cell carcinoma of the lung was found but without metastases to the central nervous system. Histology of the optic nerve showed loss of nerve fibres and myelin, together with patchy areas of round cell infiltration. There were no metastases in the brain.

It is intended to report this case fully elsewhere.

Complete Heart Block with Stokes-Adams Attacks Treated by Indwelling Pacemaker

A H M Siddons MCh FRCS MRCP and O'Neal Humphries MD (for A Leatham FRCP)

A man, aged 65, a retired blind-maker, had attacks in which he felt faint and occasionally lost consciousness, over six years. His pulse rate had been known to be about 40 throughout this period. He had no cardiac pain. Attacks had not been more frequent than one or two a week until February 1960 when they increased to several a week.

Investigations revealed complete heart block. No other cardiac abnormality was detected.

In spite of hospital treatment with ephedrine, adrenaline, isoprenaline and prednisone, the attacks became more frequent, and were observed electrocardiographically to be associated with asystole for up to 20 seconds. He became lethargic and confused.

An electrode-catheter was passed by a vein to lie within the right ventricle. A suitable monophasic electrical stimulus conveyed to the heart by this means was followed by a heart beat so that the heart could be driven at a normal rate, and for the eleven hours for which this was maintained he had no attacks. Moreover, his mental state improved for this period.

When the electrode was removed the pulse rate slowed, dropping steadily until after ten days it reached a rate of 20 to 24. Consciousness was maintained with this slow rate, but he was confused and lay inert in bed. The electrode-catheter was passed into the heart again, and pacing at 80 resulted in immediate improvement in his general condition.

Operation for Insertion of Pacemaker

On March 31, 1960, under general anæsthesia, the pacemaker was placed within the rectus sheath with a specially devised lead running from it to a metal electrode 1 cm in diameter which was attached to the left ventricle within the pericardium (Fig 1). This apparatus produced an impulse 90 times a minute (approx. 2 volts for 1·5 msec) (Fig 2).

The patient left hospital five weeks later, taking no drugs, and has led an active life since. He attends hospital for one night each week for the pacemaker to be recharged. This consists of having a light coil of wire strapped to his abdomen. A suitable alternating current is passed through this coil which recharges the accumulators of the pacemaker within his rectus sheath. The patient states that he is quite unaware of the pacemaker, not being conscious of it even when it is being recharged.

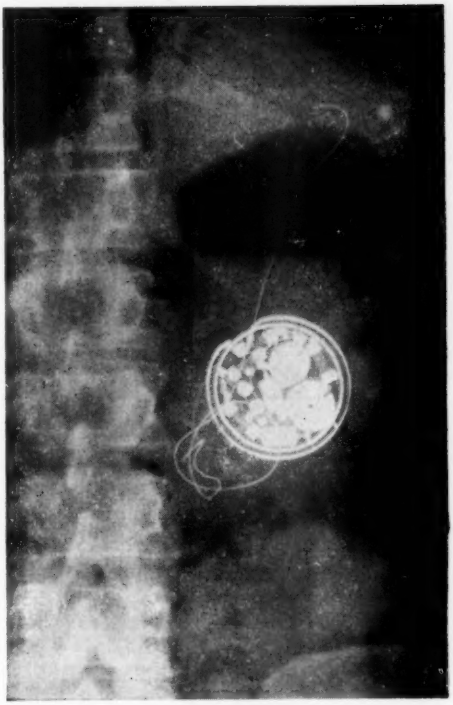

Fig 1 *Abdominal X-ray showing pacemaker in abdominal wall with leads to the heart*

The pacemaker used in this patient was made and designed by Dr Elmquist (Elmquist & Senning 1960) in Sweden. The source of energy is a small nickel cadmium accumulator used to operate a pulse generator in the form of a blocking oscillator. The whole apparatus, which is disc-shaped, is about 5 cms in diameter and 1·5 cm thick, and is embedded in inert plastic. Although in this man it has worked faultlessly for eight months, as a result of failures in other cases we are not satisfied with the design and both Dr Elmquist and we ourselves hope to produce a more satisfactory instrument.

It seems essential that, whatever method is used, no wire should traverse the skin, for if a wire is led externally there is always the danger of sepsis tracking along the wire to the heart, where it has been found to interfere with the electrical conduction.

In St. George's Hospital Cardiac Department, Mr J G Davies has been experimenting with transmission of the impulse at radio-frequency from a small external transmitter to a receiver placed in

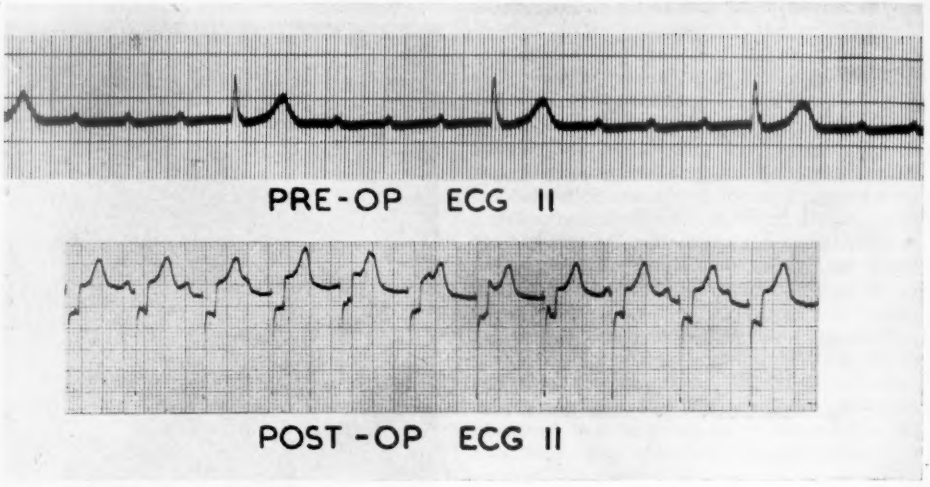

Fig 2 *Lead II of the ECG taken on admission to hospital, and after the pacemaker had been inserted. Longer recordings taken on admission demonstrate the pattern of complete heart block. Evidence of atrial activity is to be seen in both recordings*

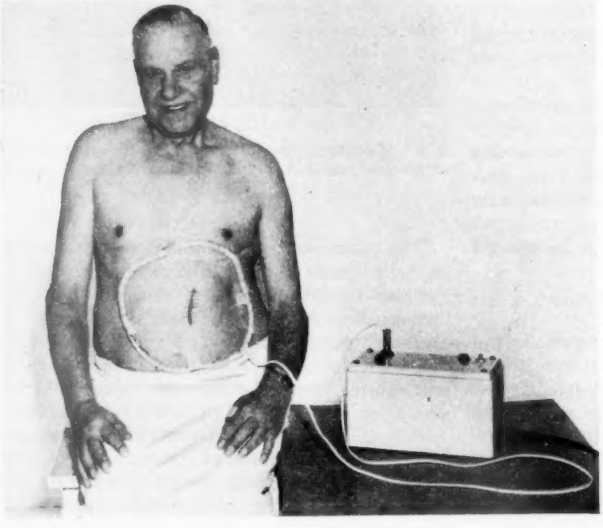

Fig 3 *The patient with the charging induction coil strapped on to the abdomen for charging*

the pericardium, and in the meantime Abrams and his colleagues in Birmingham have used the principle of induction of the impulse in to a subcutaneous coil (Abrams *et al.* 1960).

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Abrams L D, Hudson W A & Lightwood R (1960) *Lancet*, i, 1372
Elmquist R & Senning A (1960) Proc. II Int. Conf. Medical Electronics, Paris, 1959. London, p 253

The following cases were also shown:

Colonic Replacement For Impassable Stricture of the Œsophagus

Martin Birnstingl MS FRCS

Infected Cyst of the Liver

P E B Holmes FRCS (for H Park FRCS)

Symptomless Chronic Empyema

A E Stevens MB MRCP (for K P Ball MD MRCP)

Two Cases of Multiple Nævi

(1) E J Moynahan MD FRCP

(2) E J Moynahan MD FRCP (for P E Polani MD MRCP)

These cases showed somatic and psychic infantilism with delayed puberty and fibroelastosis of the heart.

Section of Odontology

President R V Bradlaw CBE FRCS FDS RCS

Meeting November 28 1960

Symposium on the Use of High Speeds in Cavity Preparation

Technical Aspects of High Speed Handpieces [*Abridged*]

by Richard R Stephens BDS MRCS LRCP (*London*)

The use of ultra-high speeds for cavity preparation, for long theoretically desirable, became a practical possibility with the development of the miniature high precision ball race, this type of bearing being now employed both in belt and pulley type ultra-speed handpieces and for those with turbine drives.

A wide variety of valve release systems, both mechanical and electrical, are now utilized to control coolant and air supplies, the non-electrical type being preferable for use in the presence of volatile anæsthetics.

Since ball races have been the bearings of choice, provision of lubrication has been essential, the lubricant being fed into the air supply in various ways. It is desirable to avoid the exhaust of oil-laden air into or near the mouth. This has been achieved by the incorporation of filters into the handpiece or control box and, on one handpiece, by the use of grease lubricated bearings.

It is hoped that air bearings not requiring lubrication will be developed in the future for ultra-speed turbine handpieces since these could help to reduce noise and could have a longer life. Noise also might be decreased by improvements in design of rotor blades. It is even possible to dispense entirely with blades and to have a miniature reaction type rotor with compressed air delivered to a central recess and exhausted through orifices at a tangent to its periphery, a rotor of this type being likely to produce less noise.

Considerably higher torque characteristics with some sacrifice of speed can be obtained by the use of a form of vane motor in place of the turbine type rotor in the handpiece head, with vanes sliding in and out of radial grooves to allow rotation of an off-centre rotor.

Up to the present time, insufficient attention has often been paid by the designers to the provision of adequate coolant supplies. The single water jet, as in the original Borden pattern handpiece, is inadequate for a number of reasons.

It may be deflected from the cutting surface by a cavity margin indicating that at least two orifices are imperative. Much of the water from a single jet is immediately thrown off by centrifugal force. Moreover, when burs or diamonds with long cutting surfaces are used portions of the cutting point may well be some distance from the point of impact of the jet and thus be inadequately cooled. When cutting points with short shanks or short necks are used, to give the advantages of miniature handpieces, the jet may even completely miss the cutting point.

If any part of an uncooled bur or diamond instrument or its shank touches enamel or dentine there is not the slightest doubt that heat production will be very great indeed and certainly must be damaging to the dental tissues.

This may readily be demonstrated by prep...ng cavities in teeth using ultra-speed handpieces in total darkness. If a tooth is cut with a turbine handpiece spinning a bur at 300,000 revolutions per minute at a pressure of only 30 g, a delicate touch in clinical practice, the glowing of white and orange light flickering through the tooth from the point of contact of the bur may be observed.

It is now evident that coolant supplies in the form of sprays are preferable to water jets in that they may provide effective cooling with ejection of much less water into the mouth. A spray has a further advantage over a jet in that it may be arranged to diverge from its orifice to envelop the whole surface of the cutting point which may thus revolve shrouded in a mist of droplets. In this

case heat production is probably satisfactorily controlled.

From a technical viewpoint it is apparent that many of the present drawbacks of ultra-speed handpieces, such as the emission of oil-laden air, bearing wear and breakdown, the complexity of their control systems, and to some extent their distressing noise, may now be overcome, but it is clear with many patterns of ultra-speed air turbine handpieces that until modifications have been made to provide more efficient cooling arrangements there is an ever present hazard of severe heat production in the tooth which is being treated.

[This lecture was illustrated by thirty-one slides.]

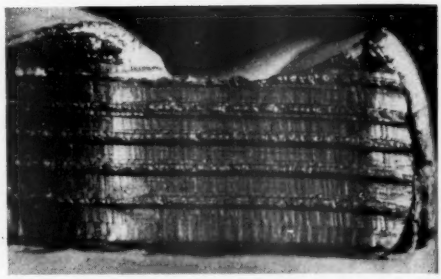

Fig 1 *Ridges on enamel surface left by No 3 cross cut fissure bur at ultra-speed. The surface has been treated with colloidal graphite*

Clinical Aspects [*Abridged*]

by G A Morrant BDS DDS (*London*)

The stage of critical assessment of the merits and demerits of high-speed cavity preparation has now been reached. A recording made by placing a throat microphone at the angle of the mandible and over the temporomandibular joint during a molar crown preparation demonstrates the great reduction in bone conducted noise and vibration perceived by the patient compared with conventional instruments (the recording was then played).

Operating time, discomfort for patient and fatigue for operator are all reduced. It is now possible to open the pulp chamber of an acutely tender, abscessed tooth without any form of anæsthetic.

Using a normal cutting pressure of 2–3 oz (70 g) an air turbine removes about eight times as much tissue in the same time as a conventional carbide bur of similar size at 10,000 rev/min and 1½ lb (0·7 kg) pressure.

The ease of cutting then, makes the ultra-speed handpieces particularly suitable for undertaking the major part of the preparation of medium and large cavities, or crowns, requiring the removal of a considerable quantity of hard tooth tissue, but for large amounts of soft carious dentine, hand excavators or large round burs in conventional handpieces are usually more efficient and certainly safer if in close proximity to the pulp. Perhaps even a 10 : 1 speed-reducing handpiece may be of use, especially if a speed-increasing wrist-joint is fitted to the engine arm. Many operators also revert to slower conventional rotary and hand instruments for completing the final outline of the cavity and finishing the margins, but before discussing the reasons for this, the finish left by ultra-speed instruments on enamel may be noted.

Cross-cut fissure burs produce gross longitudinal ridges upon the surface (Fig 1). Diamond

Fig 2 *Enamel surface cut by long tapered diamond stone at ultra-speed. Markings stained by colloidal graphite*

instruments leave well-defined score marks (Fig 2). The old pattern plain-cut fissure bur, however, produces a comparatively smooth surface with a few longitudinal scratches and some cross striations (Fig 3). This surface roughness is only of significance in inlay and crown preparations. Indeed in amalgam cavities Menegale *et al.* (1960) have shown that roughness of the walls may actually reduce permeability around the restoration. Of

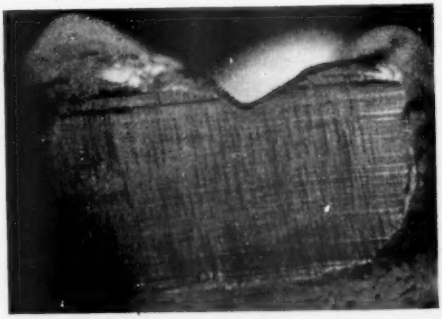

Fig 3 *Enamel surface cut by No 3 plain cut fissure bur at ultra-speed. Markings stained by colloidal graphite*

Fig 4 *Axial cavo-surface margin of cavity prepared with ultra-speed cross cut fissure bur*

Fig 5 *Axial cavo-surface margin prepared with ultra-speed diamond*

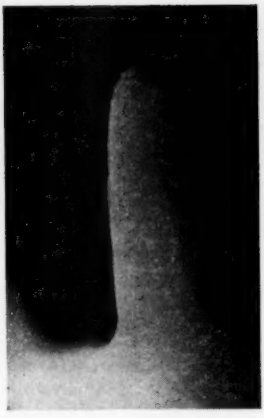

Fig 6 *Axial cavo-surface margin prepared with ultra-speed plain cut fissure bur*

greater importance is the finish of the cavity margins. Both the cross-cut fissure bur (Fig 4) and the ultra-high-speed diamond (Fig 5) compare unfavourably with the plain-cut fissure bur, which leaves a reasonably smooth margin (Fig 6).

Although an acceptable finish is thus possible, stepping of both axial and gingival margins (Fig 7) is difficult to avoid in some situations. This is also the case with the shoulders of crown preparations. Recourse is therefore usually made to slow rotary or hand instruments for completing the cavity preparation.

Many operators are also disinclined to use the turbine handpiece on small anterior cavities where extension into sound tooth structure must be minimal. The difficulty of control already referred to may be accentuated by the slightest eccentricity in the chuck, which results in an oversize cavity in the tooth.

In the anterior region again indirect vision of palatal surfaces is perhaps even more difficult than elsewhere in the upper jaw. The fogging of mirrors by droplets may be reduced by dipping the mirror in a detergent solution, but an air-driven rotary mirror is probably more effective, although unfortunately it is not a complete answer and there are additional difficulties in using one in the posterior region.

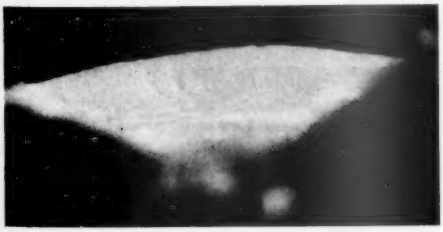

Fig 7 *Occlusal view of gingival margin of cavity prepared with ultra-speed fissure bur*

Removal of coolant from the mouth may present a problem. Efficient mechanical suction is one answer. Better still is the use of a spray as advocated by Mr Stephens.

Thermocouple studies present a number of difficulties but a limited number of measurements on a tooth with an occlusal fissure cavity filled with amalgam, one end of which is in contact with a thermocouple, shows that removing the amalgam dry with a carbide bur records a maximum temperature of well over 70° C. The interesting point is that this temperature is attained during the initial penetration and subsequently reduces when running out the fissure towards the thermocouple. However, either jet or spray at approximately 30 ml/min keeps the temperature down to 35° C. It would appear that the greatest danger of overheating comes from plunge cuts with turbines and it may be wise to open up cavities over a wide area without deep penetration at any one point.

Acknowledgments: Mr Stephens and Mr Morrant would like to express their thanks to the laboratory technicians and the photographic staff of the Institute of Dental Surgery, Eastman Dental Hospital, for their help in the above research work and in the presentation of the Symposium.

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[A fuller account of some of the subject matter of these papers by R R Stephens and G A Morrant may be found in serial form in the *British Dental Journal*, 1960, **109,** Nos. 1–12, beginning on p 5.]

Air Contamination from High-Speed Dental Drills

by G Kazantzis MB PhD FRCS (*London*)

The human respiratory tract possesses defence mechanisms which offer considerable protection against inhaled particles and aerosols. Some large particles are filtered by the hairs within the nasal cavity. Others, coming into contact with the mucous membrane of the pharynx and larynx, excite the cough reflex, and are expelled, enveloped in mucus. Smaller particles which enter the trachea and bronchial tree may come to rest on the mucosa, or may be carried to the respiratory bronchioles or the alveoli of the lung. However, not all inhaled particles are arrested by the lung. A high percentage of sub-micron particles remain entrained in the airstream, and are expelled during expiration. The arrested particles are rapidly enveloped in mucus secreted by the goblet cells of the bronchial mucosa. Some are expelled mechanically by the rhythmical beat of the ciliary epithelium, whilst the remainder are engulfed by phagocytes, and again, may either ascend this 'ciliary escalator' or else may be transported through the epithelial lining into the lymphatic system, to be deposited in regional or more distant lymph nodes. Different inhaled materials excite the phagocytic response to different degrees, and studies of the clearance rates of inhaled particles are now going on.

Alveolar deposition and retention of inhaled particles is determined mainly by their size and shape. Maximal retention takes place with particles from 0·5–5 μ in diameter, although the diameter is not the critical parameter of the particle, recent work suggesting that deposition is mainly dependent on its terminal velocity. Particles greater than 25 μ in diameter are not often seen in the alveoli, even though the diameters of these may be 80–130 μ.

Whether inhaled particles are injurious or not depends, therefore, not only on their composition, concentration and duration of exposure, but also on their size and shape. When a dental drill is used, particles are produced from the tooth – enamel, dentine, cement, carious material, bacteria and old filling materials, and also from the bur – particles of steel, tungsten carbide and diamond, although the latter will be present in very low concentrations. To all the foregoing particles droplets of water and lubricating oil are added when the air turbine is used. Small particles remain suspended in room air for many hours after their emission, and are rapidly distributed over the room as a whole by small air currents. When oil and water droplets are produced close to the source of solid particles, these and oil droplets will be found within water droplets. This will have the effect of aggregating the smaller oil droplets into larger drops, and the solid particles into larger masses, which may, however, break apart again when the water droplet dries.

In the survey performed by the Department for Research in Industrial Medicine, the air turbine drill was found to be used in a number of different ways. The investigation was restricted to an N.H.S. practice, and to the Dental Department of a London teaching hospital. The drill was seen to be used both dry (although not in the hospital), and with a water jet. The water supply being variable, the drill was sometimes used with much water, and sometimes with very little. The oil supply was also variable, and on different machines the oil drip feed rate was found to vary between 28 and 78 drops per minute. Vegetable oils, such as olive oil, almond oil, and coconut oil, are most frequently used to lubricate the turbine, but paraffin oil, which is a mineral oil, is also used to-day. The vegetable oils contain a stabilizer to prevent oxidation and increase in viscosity of the oil film.

Observation of the oil spray, at the drill head of an 'Alston' portable instrument, showed variations dependent on the oil drip feed rate. Immediately after a drop had been observed in the counting chamber, a fine mist of oil droplets was visible in a beam of light close to the turbine head. This mist decreased in intensity until the next drop was seen to fall. The mist was composed largely of droplets of about 0·5μ diameter, but there were also some larger drops.

Atmospheric sampling was performed with the drill used 'dry' and 'wet', first on a model, and then at the chairside. The model was a brass cylinder 6 cm in diameter and 7 cm long, with the remote end sealed, in which four teeth were mounted. These were drilled continuously for 30 minutes with the 'Alston' portable instrument, both with and without a water jet.

The oil flow rate was 33 drops per minute, and the water flow 2·6 ml per minute. An air sample taken at a point one foot in front of the 'mouth' and six inches above it showed an average oil concentration of 1·3 mg oil per cubic metre of air. A second sample, taken during ten minutes of drilling showed a calcium concentration from the tooth particles of 0·10 mg per cubic metre of air. However, when the drill was used without a water jet, the calcium concentration was 1·5 mg per cubic metre of air, or 15 times the concentration attained when using the water jet. In practice, the drill would not be used for such a long period of time, so that the concentrations obtained would be lower. Microscopic examination of a cascade impactor sample showed that the greater mass of

the oil and particulate matter was trapped in drops of water larger than would usually be considered respirable.

Samples were taken at the chairside, as close as possible to the operator's face (Fig 1). A fine cloud of droplets could be seen close to the patient's mouth during drilling. While the attempt was made to sample within this cloud, it was by no means always possible, owing to the short time that it was visible, and to its rapid dispersal a short distance in front of the patient's face. The actual drilling time in the preparation of a cavity was rarely found to exceed 90 seconds. Samples taken when the drill was running without water showed an oil concentration of 0·62 mg per c.m and a calcium concentration of 0·047 mg per c.m of air. These concentrations were approximately halved one yard away. For comparison, oil concentrations in the general atmosphere of a machine shop, where semi-automatic lathes were used, averaged 0·5–1·0 mg per c.m throughout the day.

Samples of oil and water droplets, and solid particles taken by means of a konimeter are shown in Fig 2. Oil droplet counts varied from a few to 180 per c.c, with an average size of one micron, but with some droplets greater than 10 μ. Solid particles varied from a very few to 170 per c.c, the average size being 1·5 μ, with occasional particles up to 150 μ.

Fig 1 *Atmospheric sampling at the chairside, using a konimeter, during the use of a high-speed dental drill*

Samples were taken in the same way while a conventional drill was in use. The concentration of solid particles during drilling was very small, but when an air syringe was used to blow out the debris in the cavity, a very much higher concentration of particles was obtained than at any time during drilling with the high speed instrument (Fig 3).

Observations on bacterial contamination during the use of the high speed drill were made by drawing air from the region of the operator's face through a slit sampler, and impinging this on a

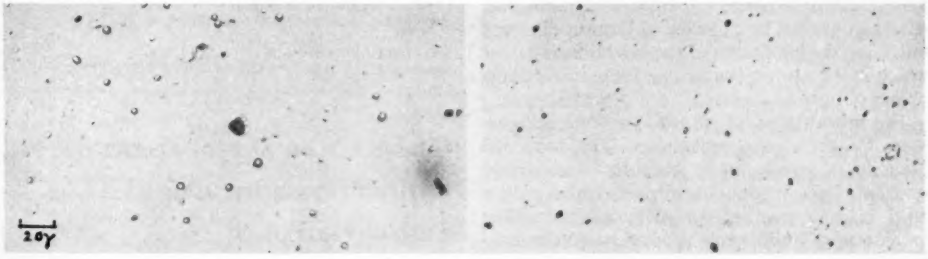

Fig 2 *Samples of oil and water droplets and solid particles*

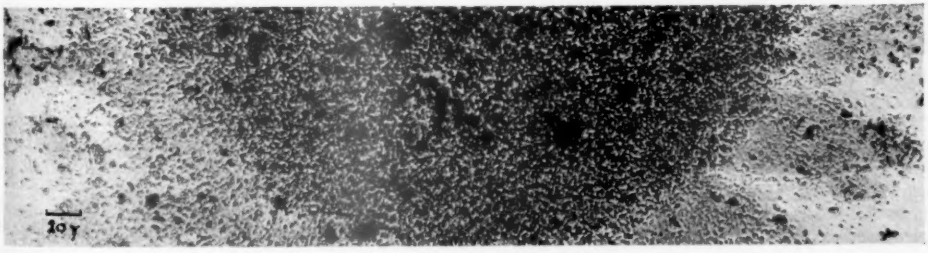

Fig 3 *Samples of solid particles taken after blowing out with an air syringe*

rotating blood agar plate. Samples were taken before, during and after drilling with both high speed and conventional instruments. The periods during which drilling was performed could be identified on the plates as tooth debris could be seen in the appropriate segment. A uniform distribution of aerial contaminants was seen, the predominant organisms being *Staphylococcus albus* and a Gram-negative bacillus of the aerogenes group. Some periods of drilling were associated with a growth of *Streptococcus viridans* organisms. These were found following the use of both high speed and conventional drills, and were the only organisms to be specifically associated with drilling procedures, although sampling was related to a number of patients on different days in the two dental surgeries investigated.

From these observations, it was thought that there was no increased risk to the operator of bacterial contamination associated with the use of the high speed drill. It was found that the quantity of respirable dust produced by the high speed drill was small, especially when it was used with a water jet, and when not only the concentration, but also the total time of exposure to the peak concentration was taken into account.

Consideration of the composition of the solid particles does not reveal the presence of any substance that might be considered to be pathogenic in the concentrations encountered. The silicates found in amalgam fillings do not have the same fibrogenic properties as free silica, and pathogenic effects would not be expected to occur in the lung following the inhalation of the crystalline apatites which make up the enamel, or the calcium phosphates of bone.

The introduction of oil into the lung is, however, by no means innocuous. Oils have the capacity of producing a granulomatous tissue reaction with surrounding fibrosis, producing a hard mass known as an oleogranuloma. The inhalation of animal oils produces an inflammatory reaction in the lung with many multinucleated foreign body giant cells and large mononuclear cells with oil laden cytoplasm. A dense wall of connective tissue may in time be laid down round these clusters of cells. The reaction may be acute and produce pneumonic consolidation followed by resolution. Such lesions have been demonstrated in children who have inhaled cod-liver oil.

Mineral oils produce a slower but intense fibrous tissue reaction surrounding collections of oil laden macrophages. Firm masses develop in the lung which may superficially resemble a malignant lesion, termed descriptively, a paraffinoma. Chronic respiratory symptoms are often produced. Many such cases have been described following the inhalation of liquid paraffin administered medicinally (Ikeda 1937, Proudfit *et al.* 1950, Symmers 1955, Forbes & Bradley 1958).

Vegetable oils, if free from fatty acids, rarely produce an inflammatory reaction in the lung. The oil droplets are usually broken up and removed via the lymphatic system by phagocytes, so that eventually no trace of oil is left. Iodized vegetable oils are commonly introduced into the lung for radio-diagnostic purposes, and ill effects associated with these oils have rarely been reported (Pinkerton 1928, Santé1949).

It is recommended that vegetable oils free from impurity should be used exclusively for lubricating purposes in air turbine drills. The minimum quantity compatible with efficient running of the machine should be used. If the instrument is used with a water jet there will be an appreciable reduction in air contamination with solid particles, so that apart from any consideration concerning the safety of the tooth operated upon, the safety of the dental surgeon operating the drill is also made more certain.

Acknowledgments: I would like to thank Professor C F Barwell for bacteriological facilities and for interpreting the bacteriological sampling results, Dr A I G McLaughlin for his generous advice, and Mr E King for performing the atmosphere sampling tests.

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Changes in the Dental Tissues due to Cavity Preparation using a Turbine Handpiece

by Ivor R H Kramer MDS FDS RCS (*London*)

Two years ago it was decided to investigate the tissue changes that might follow cavity preparation using a turbine handpiece. The main purpose was to determine the effects of such instrumentation upon the pulp. However, unexpected findings during the course of the investigation led to a widening of the scope of the experiments, firstly to include changes that were observed in the dentine, and more recently to explore the possibility of changes in the enamel.

For the investigation into changes in the pulp, it was thought desirable to use both diamond points and tungsten carbide burs, and to compare the response following cutting under waterspray

with the response that followed cutting with no waterspray. Consequently, there were four experimental groups, the two main groups according to the type of cutting point, each divided again according to whether or not waterspray was used. In addition, a fifth group of experiments was included, not strictly speaking a control group, but rather a basis for comparison. In this group, the cavities were prepared using steel burs under waterspray in a conventional handpiece.

For the turbine handpiece experiments, Borden airotor handpieces were used. The rotary speed whilst cutting under an average load was found to be about 320,000 rev/min. Cavity preparation was carried out with cylindrical diamond points, or tungsten carbide cross cut fissure burs of comparable size. All the cavities were prepared in non-carious teeth in young individuals, and unless immediate extraction was intended the cavities were filled with zinc oxide and eugenol. The experiment duration (i.e. the interval between cavity preparation and extraction) ranged from a few minutes to 231 days, and the cavities varied in depth from those barely penetrating the dentine to pulpal exposures.

In order to assess the tissue changes that had occurred, paraffin sections were prepared and records were made of various types of deviation from the normal. In this report, reference will be made to five types of change, and the percentage of experiments in each group in which these changes were found is shown in Table 1.

Table 1
Percentage incidence of pulpal changes

	Turbine handpiece				*Conventional handpiece*
	Diamond		*Carbide*		*Steel*
	Wet	*Dry*	*Wet*	*Dry*	*Wet*
Inflammatory cell infiltration	37	48	24	39	38
Secondary dentine formation	17	65	0	65	9
Œdema	10	31	12	16	0
Coagulation	2	4	0	11	0
Odontoblast 'aspiration'	10	31	16	57	0

The figures for secondary dentine formation relate to experiments of more than 14 days' duration and those for odontoblast 'aspiration' to experiments of up to 32 days' duration

Pulp Changes

Infiltration of the pulp with inflammatory cells was a relatively common finding. Almost always, the infiltrating cells were lymphocytes. Only occasionally were polymorphonuclear leucocytes found, even in the experiments of short duration. The percentage of experiments in which inflammatory cell infiltration was found was a little higher in the groups in which no waterspray was used, but there were no striking differences between the groups; also, there was no striking difference between the turbine experiments and the experiments in which the conventional handpiece was used.

Secondary dentine formation indicates both stimulation of the pulp, and the capacity of the pulp to respond. In most of the experiments the secondary dentine was well formed, although in some teeth vascular loops had been partially included in the newly formed hard tissue (Fig 1). The incidence of secondary dentine formation varied markedly from one group to another, with a notably high incidence beneath the cavities cut without waterspray.

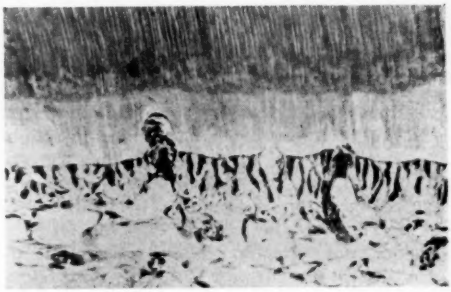

Fig 1 *Vascular loops in predentine. H & E* × *170*

In a previous report, on the response of the pulp to a self-polymerizing resin (Kramer 1956) reference was made to a curious disturbance of the fluid balance in the region of the odontoblast layer, and a somewhat similar change was found in some of the teeth in the present series. The incidence of this type of change, a pulpal œdema, was low in most of the groups, although in one group, with dry cutting, almost a third of the teeth showed some degree of œdema.

It is well known to dental histologists that, in many sections of teeth, part of the pulp stains very deeply with eosin. This appearance, almost always seen in the cornu, is regarded as an artefact. However, in some of the present experiments, part of the pulp lying, not in the cornu, but beneath the experimental cavities, showed a granular structure and a strong affinity for eosin, and it is considered that this may represent a coagulation of the pulpal tissue due to heat. Few teeth showed this appearance, but almost all of them were in the groups in which the cavities were prepared dry.

The passage of odontoblasts, or odontoblast nuclei, outwards from the periphery of the pulp into the dentinal tubules has been observed under a wide variety of experimental conditions, and both the mechanisms responsible for this so-called 'odontoblast aspiration' and its significance are controversial matters (Stanley & Swerdlow

1958, Kramer 1959). This odontoblast aspiration was not seen at all beneath the cavities prepared using a conventional handpiece, and in the turbine handpiece experiments the incidence of aspiration was obviously higher in the groups in which the cavities were prepared without waterspray.

If all these results are placed together, it will be seen that the high figures for various pulp reactions all occur in the groups in which the turbine handpiece was used without waterspray. These results, based on almost 200 experiments, clearly support the view that the use of an efficient cooling mechanism is desirable if the risk of pulpal damage is to be reduced.

Dentine Changes

During the course of these investigations into pulp response, changes were seen in the dentine of some teeth (Kramer 1960). In sections of teeth in which cavities have been prepared with a conventional handpiece, the dentine next to the cavity floor has the same appearance as the dentine elsewhere. However, in sections of some teeth in which cavities were prepared with a turbine handpiece, the dentine forming the cavity floor had a markedly abnormal appearance. These changes were of two degrees. The more severe, termed dentine 'burning', showed a swelling of the matrix, a loss of affinity for hæmatoxylin and eosin, and a tendency to dissolve away. Sometimes, fusiform dilatation of the dentinal tubules and small rounded spaces in the matrix suggested that gas bubbles had formed. The less severe change was characterized by an increased affinity of the affected dentine for hæmatoxylin, and this was termed dentine 'darkening'. Special staining and impregnation techniques provided confirmation of the view that, in the affected areas, a breakdown had occurred in the collagenous dentine matrix, whilst further investigations showed that all the changes could be reproduced by the application of heat to the dentine (Kramer 1960).

The severe changes were never seen beneath cavities cut using conventional handpieces, and the incidence was high (61%) in the group in which the turbine handpiece was used with the carbide bur but without waterspray.

The less severe heat change was found in about 80% of the teeth in which cavities had been prepared using the turbine handpiece without waterspray, but, of particular interest, in one group half the teeth showed this effect although waterspray was used.

The distribution of the heat changes was studied, and it was found that two areas tended to be affected (Fig 2). One area was in the cavity floor, and presumably showed where heat generated by the end cutting component of the bur or

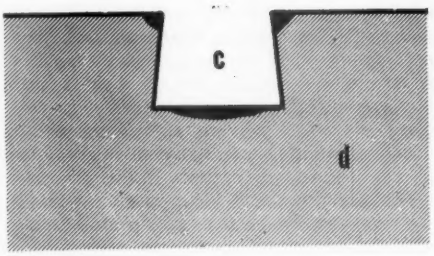

Fig 2 *Diagram of decalcified section of tooth showing distribution of heat changes. c – cavity. d – dentine*

diamond was inadequately dissipated because the water did not reach that region in sufficient quantity.

The other area tending to be affected was in a wedge-shaped mass of dentine in the region where the cavity wall crossed the amelodentinal junction (Fig 3). The presence of heat changes in the dentine in this area suggested that the effect might be the result of considerable heat generated in the overlying enamel during cavity preparation. The heating of the enamel may have a practical importance, for it seems at least possible that the enamel might be rendered more fragile, and consequently more liable to break away from the margins of the restoration.

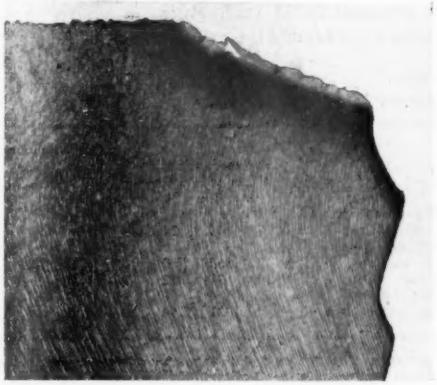

Fig 3 *Decalcified section showing heat changes in dentine in region where cavity margin (right) crosses amelodentinal junction. H & E × 56*

Heat Rise in Enamel

The measurement of heat rise during cavity preparation in this narrow zone in the enamel would be very difficult if conventional methods, such as thermocouples or thermistors were used.

Therefore, this problem has been investigated by an entirely different approach, and recently a paper by Wheatcroft *et al.* (1960) reports investigations using a very similar technique.

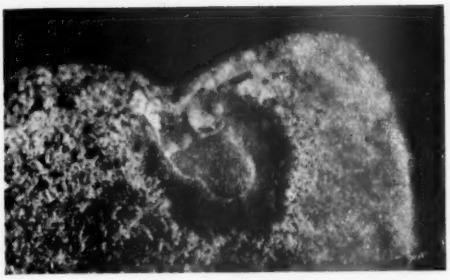

Fig 4 *Tooth with dyed enamel surface covered with powdery heat-sensitive coating fusing at 101° C. A small cavity has been cut with an uncooled bur in a turbine handpiece, and round the cavity there is a zone in which the coating has melted*

It is possible to cover the enamel surface with an adherent powdery coating of a material that melts at a known temperature. If, now, a cavity is cut into the tooth substance, a rise in temperature above the melting point of the coating will cause the coating to melt in the heated zone, and this melting can afterwards be recognized by the change in the texture of the coating from matt to glossy. Unfortunately, on the enamel the change is not easy to see, and is even more difficult to photograph. The change from matt to glossy occurs because, when the melting point is reached, the powdery particles fuse together. Because of this, the coating changes also from opaque to transparent. Therefore, if the enamel surface is coloured first, and this can be done quite simply with any convenient dye, then this coloured surface will be obscured when the powdery coating is applied. If a cavity is now prepared, areas in which the coating has melted will be easily seen because the coloured enamel surface will show through the fused coating. [A film was shown illustrating this technique.]

Much of the preliminary work has been done with a coating that melts at 101° C, and Fig 4 shows a tooth studied in this way. It will be seen that, in a narrow zone around the cavity margins, the temperature of the enamel has reached at least 101° C.

This technique of investigating heat generation during cavity preparation is now being used in a variety of ways, but the results so far provide further support for the view that cavity preparation using a turbine handpiece will almost certainly cause considerable heating of the tissues unless water, or some other cooling mechanism is used. Provided there is adequate cooling, all the results from the present investigation indicate that no serious damage is likely to be inflicted upon the dental tissues.

Acknowledgment: The author is indebted to Mr G A Morrant for his collaboration in this investigation, to the laboratory and photographic staff for their invaluable help, and to the Editor of the *British Dental Journal* for permission to reproduce Figs 2 and 3.

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Stanley H R & Swerdlow H (1958) *Oral Surg.* **11**, 1007
Wheatcroft M G, Hartnett J E & Smith W E
(1960) *Dental Progress*, **1**, 52

Meeting October 24 1960

Mr R V BRADLAW delivered his Presidential Address entitled **E Tenebris.** The Address was illustrated by coloured slides and demonstrations.

Books received for review

Armitage P
Sequential medical trials
pp 105 20s
Oxford: Blackwell 1960

Bluefarb S M
Leukemia cutis
American Lecture Series No 354
pp xxvi+489 £7 8s
Springfield, Ill.: Thomas
Oxford: Blackwell 1960

Bluefarb S M, ed
Cutaneous manifestations of the reticuloendothelial granulomas
American Lecture Series No 363
pp xiv+442 £5 16s
Springfield, Ill.: Thomas
Oxford: Blackwell 1960

Bluefarb S M ed
The cutaneous manifestations of the benign inflammatory reticuloses
American Lecture Series No 378
pp xviii+408 £5 12s
Springfield, Ill.: Thomas
Oxford: Blackwell 1960

Brain Sir Russell
Clinical neurology
pp viii+399 38s
London &c: Oxford University Press 1960

Brock J F
Recent advances in human nutrition
pp xii+454 50s
London: Churchill 1961

Colmeiro-Laforet C
Educación, sexo y sexualidad
pp 185 150 ptas
Vigo: Faro de Vigo 1961

Roberts F
Good English for medical writers
pp ix+179 17s 6d
London: Heinemann 1960

Schreiber G
Embolic dispersoids in health and disease
American Lecture Series No 390
pp xvi+85 44s
Springfield, Ill.: Thomas
Oxford: Blackwell 1960

Simon H J
Attenuated infection:
the germ theory in contemporary perspective
pp xvi+349 80s
Philadelphia & Montreal: Lippincott 1960

Smith I
Chromatographic and electrophoretic techniques
Vol I Chromatography
2nd ed pp xvii+617 65s
Vol II Zone electrophoresis
pp viii+215 30s
London: Heinemann 1960

Soddy K
Clinical child psychiatry
pp x+470 42s
London: Baillière 1960

Thomas A, Chesni Y & Saint-Anne Dargassies S
The neurological examination of the infant
edited by R C Mac Keith, P E Polani and E Clayton-Jones
Little club clinics in developmental medicine No 1
pp 50 5s
London: National Spastics Society 1960

Transactions of the International Society of Plastic Surgeons
Second congress, London 1959
edited by A B Wallace
pp xxiv+589 £4 10s
Edinburgh & London: Livingstone 1960

Williams R E O *et al.*
Hospital infection. Causes and prevention
pp viii+307 35s
London: Lloyd-Luke 1960

Willis A T
Anærobic bacteriology in clinical medicine
pp xii+163+13 30s
London: Butterworth 1960

Wright S E
The metabolism of cardiac glycosides
American Lecture Series No 368
pp viii+86 38s
Oxford: Blackwell 1960

Youssef A F
Gynecological urology
pp xvii+893 £9
Springfield, Ill.: Thomas
Oxford: Blackwell 1960

Book reviews

The Chemical Senses in Health and Disease
by H Kalmus SCD MD and S J Hubbard BSC PHD
American Lecture Series No 394
pp vii + 95 illustrated 30s
Springfield, Ill.: Charles C Thomas
Oxford: Blackwell Scientific Publications Ltd 1960

This short book sets out in a very clear and readable way the salient facts concerning the anatomy, physiology and psychology of taste and smell. Nothing recondite is attempted, but the treatment is reasonably comprehensive and critical without being fashionably carping. There is a chapter on the ecological and evolutionary significance of taste and smell, that is, the place of these sensations in nature, then chapters on the mechanisms, so far as they are understood, of taste and smell. There is a glance at current and possible future research in this field, and a brief note on chemical sensation and disease. There are some seventy-five references. The book can be warmly recommended as a very pleasant evening's reading for physiologists, psychologists and clinicians of all varieties. It is excellently produced, but at 30s competes with difficulty with two and a half hours of the theatre or concert hall.

Mary Queen of Scots. The Daughter of Debate
by Sir Arthur Salusbury MacNalty KCB MA MD FRCP FRCS
pp 247 21s
London: Christopher Johnson 1960

Sir Arthur MacNalty has already established for himself a well-earned reputation as a historian: his latest work is, without doubt, one of his best and most attractive publications. There is probably no woman in history who, 'had hardly seen the light of day before she became so much the subject of men's ambitions and political intrigue, baleful influences which were to beset her throughout life'.

In this book we have, in addition to the general account of the career of this unfortunate woman, some interesting details of her various illnesses, factors which doubtless played a more important part in her life than is generally realized. Her medical case-sheet, given in the first appendix at the end of the volume, furnishes an illuminating account of the serious maladies from which she suffered, and of the inadequate means of treatment afforded by the clinical knowledge of the period.

Much has been written about Mary Queen of Scots, some of it in her favour, some to her detraction. Whatever be the whole truth, the most hard-hearted of critics cannot fail to be moved by a feeling of pity and sympathy after reading Sir Arthur's account of the suffering and distress experienced by this ill-fated Queen, whose only years of happiness seem to have been those spent in childhood and adolescence in France. For much of her later sufferings she may have been herself responsible. Her desire to be recognized by her cousin of England as heir presumptive to the English throne amounted almost to an obsession, and perhaps explains much of the difficulty in which the great Queen Elizabeth found herself and of her frequent harshness to Mary, despite her protestations of regard and affection. Of Mary's alleged complicity in the many crimes recounted in this history there have always been, and will presumably always be, different views. In this fascinating volume Sir Arthur has maintained throughout a strictly impartial and judicial attitude, giving us all the facts so far as they are known, and leaving his readers to play the part of a jury in arriving at their verdict.

The book contains a good bibliography, and an important appendix upon the notorious 'Casket Letters'. It provides a delightful and well-written account of one of the most interesting and pathetic characters in history.

Abstracts of Japanese Medicine. Vol 1, No 1, October 1960
Abstracts of the Medical Literature of Japan in the Clinical and Theoretical Fields
edited jointly by T Yoshida and J Huizinga
pp xvi + 188 Subscription $30.00 per annum
Amsterdam, London, New York: Excerpta Medica Foundation 1960

No one actively interested in medicine can resist a volume of abstracts, and as he looks at it feel other than extremely grateful for all the effort and selection that have gone into its production. There can be no question, therefore, that these abstracts of Japanese medicine will be welcomed.

There is clearly a lot of activity going on in the medical centres of Japan and there is vitality in their work. The very number of journals from which abstracts are made is an index of this and is quite remarkable.

The abstracts themselves seem to be sensibly selective in their length and unnecessary space has been denied to the less important papers. The arrangement of the volume and its production is attractive and adds to the pleasure of seeing what is going on in Japan.

Children for the Childless. A Concise Explanation of the Medical, Scientific, and Legal Facts about Conception, Fertility, Sterility, Heredity, and Adoption
edited by Morris Fishbein MD
pp xiii+210 illustrated 12s 6d
London: William Heinemann Medical Books Ltd 1960

This is not just another book on infertility. It is written by multiple authors of acknowledged authority and has been 'translated' from the original American by Mr John Stallworthy.

It is directed not only toward medical practitioners and gynæcological specialists, but educated lay people will also find it readable and informative. The transatlantic origin is obvious and is no detriment, providing a salutary lesson in the humanitarian attitude of mind toward a very sensitive problem.

A mechanistic view is carefully avoided by the authors, who are obviously aware that studies of human infertility are not to be debased to the level of animal husbandry. The importance of psychological factors having an adverse somatic effect is emphasized.

British readers may find ideas of X-ray stimulation to ovaries or pituitary do not confirm with their own. Indications for artificial insemination are discussed and are obviously rare. The authors might have finished with AIH in these 'do it yourself' days by prescribing a horn spoon in their own best tradition. The thorny legal and practical problems of AID will give the itinerant inseminator food for reflective thought.

The legalities of adoption are clearly defined and the days of a medical practitioner placing the child of an unmarried mother with adopting parents are finished.

Lymphatics and Lymph Circulation. Physiology and Pathology
by István Rusznyák MD, Mihály Földi MD and György Szabó MD
pp 853 illustrated £7
Oxford &c: Pergamon Press Ltd 1960

This monograph contains a wide variety of data on many aspects of the lymphatic system and a bibliography which is extensive but contains some serious gaps. There are interesting comparative data, and a good section on the development of lymphatic vessels. The authors favour the view that there is a centripetal growth of lymphatics, as against the centrifugal interpretation of Sabin.

Nuck's introduction of mercury injection started off a long series of investigations into the best methods for the demonstration of lymphatics. Towards the end of the nineteenth century the widespread adoption of the interstitial injection technique enabled numerous observers to obtain preparations of 'lymphatic' vessels which have formed the basis of the traditional illustrations now found in textbooks. The authors rightly regard many of these as suspect, and strongly favour non-injection techniques, involving essentially lymphatic obstruction with dilatation of vessels behind the obstruction. With this technique they confirm the existence of the spaces of Disse, and give interesting illustrations of the discharge of colloid from the thyroid via the lymphatics.

Lymphatic obstruction and lymphœdema in cases of elephantiasis are generally associated with increase in fibrous tissue. The authors believe that this is a widespread phenomenon, responsible for many cases of chronic progressive fibrosis. They suggest lymphatic obstruction as the real cause of otherwise unexplained cases of fibrotic change – e.g. of spleen and liver in Banti's disease. They believe pulmonary fibrosis may also develop in the same way.

In the case of intestinal lymph, mesenteric lymphadenitis could not only cause lymphatic obstruction but also interfere with fat absorption, and the authors consider this a probable cause of idiopathic steatorrhœa. Lymphatic obstruction in the heart produces striking changes in the electrocardiogram.

Despite some obvious defects the book contains a great deal of information concerning the lymphatic system, and will make a valuable addition to the literature of the subject.

Preventive Medicine and Public Health
An Introduction for Students and Practitioners
by Fred Grundy MD MRCP DPH
4th ed pp viii+316 illustrated 27s 6d
London: H K Lewis & Co Ltd 1960

This book has been brought up to date, and the demand for a fourth edition in nine years reflects on both the need for a work of this kind and on the appreciation of the text by students and practitioners. The new edition includes a good account of the Local Government Act, 1958, and perhaps too few details of the Mental Health Act, 1959. The findings and recommendations of the Cranbrook Committee on the Maternity Services (1959) are also dealt with rather briefly for such an important and controversial topic. The national health and morbidity statistics have been revised, bringing a much clearer picture of recent trends. The references and suggestions for further reading provide a useful guide, and serve to enhance the excellence of this book.

Cell and Tissue Culture
by John Paul MB ChB PhD MRCPEd
2nd ed pp xi+312 illustrated 32s 6d
Edinburgh & London: E & S Livingstone 1960
It is not surprising to find that a new edition of this excellent handbook has been called for within a year. Such an experience would have been impossible ten years ago, and is a measure of the growing importance and simplicity of cell and tissue culture.

Although a new chapter on transplantation, in eggs, anterior eye chamber and hamster cheek pouch for example, has been added, this noteworthy laboratory manual still has only 312 pages. Fresh material and new illustrations are also to be found, and the only danger is that the author may be tempted to enlarge subsequent editions, which will be numerous.

By all means let us have more works on special aspects of tissue culture from Dr John Paul: but let him remember that the great and continued merit of successful laboratory handbooks, such as 'Mackie and Macartney' has been the happy combination of brevity and competence.

Radiation Injury in Man. Its chemical and biological basis, pathogenesis and therapy
by Eugene P Cronkite MD and Victor P Bond MD PhD
American Lecture Series No 382
pp vii+200 illustrated 52s
Springfield, Ill.: Charles C Thomas
Oxford: Blackwell Scientific Publications Ltd 1960
According to the publisher this book is designed for the practising physician, for science and biology teachers in high school and college, for medical students, for technicians and for other interested individuals. In the event the authors seem to have addressed themselves to the reader with medical experience but unfortunately the book cannot really be recommended even to him. Half the book deals with the effects of single exposures to large doses of radiation and only the last fifth of it considers the long-term somatic and genetic effects of irradiation. Besides this serious lack of balance and a number of factual errors, the arrangement and writing are often poor. In a book for the non-specialist, discussion of wholly discredited hypotheses (one is referred to in three separate places) can only confuse, and the frequent grammatical mistakes are sometimes misleading, e.g. 'the interference of mitosis in the orderly renewal of many tissues' (p 75), where what is meant is 'the interference with the mitosis which is normally responsible for the orderly renewal of many tissues'. Cf also 'In all such accidents (exposures to radiation), the physician of course played a prominent role' (p 10).

There is indeed a 'current need for a semi-technical, or non-technical presentation of basic and practical material necessary for an understanding of the effects of ionizing radiation on man', but the present volume has not provided it.

Medical and Dental Aspects of Fluoridation
by W A Cannell MRCS LRCP DPH LDS RCS
pp vii+125 15s
London: H K Lewis & Co Ltd 1960
The Fluoridation of the title is that of drinking water and is performed for the prevention of dental caries in persons who drink the water as children. This book is not a study of the value of the procedure as indicated in the well-known investigations and demonstrations: it is rather a broad description of the nature of the whole problem, both in relation to teeth and to all aspects of health. The author has gathered and summarized a mass of relevant information from scattered sources and has thus made it possible for the professional man to obtain with little trouble a considerable measure of understanding of a question upon which his opinion may well be sought. The material is presented without prejudice and with caution. This little book deserves to be widely read.

Calcium Metabolism and the Bone
by Paul Fourman MD DSc FRCP
pp 325 illustrated 37s 6d
Oxford: Blackwell Scientific Publications Ltd 1960
For over a decade, the classic monograph of Albright and Reifenstein has been the standard work in the English language on metabolic bone disease. Its authority has been such that even contributions on the subject to multiple author textbooks have tended to be a reflection of Albright's and Reifenstein's views. While the contribution of these American workers to the development of this field will always remain an outstanding one, the need for a more conventional, more systematic and less persuasive textbook has long been felt. Dr Fourman has gone a long way to supplying this need. This is an unpretentious but well balanced and reasonably comprehensive survey of a field which is growing in importance. It reveals a genuine understanding of both physiological and clinical considerations as would be expected from an author with Dr Fourman's record. It cannot be said, nor would Dr Fourman claim, that this work represents a major original contribution to the understanding of calcium metabolism, but it is a reliable and well-written text ideally suited for post graduates and practising clinicians.

A Short History of Obstetrics and Gynecology
by Theodore Cianfrani MD
pp xvi+449 illustrated £5
Springfield, Ill: Charles C Thomas
Oxford: Blackwell Scientific Publications Ltd 1960

This is a book of some 400 pages of good type and easy reading. It covers the development of obstetrics and gynæcology from its earliest source up to our own time – a feat of some magnitude in such small space – and although a great deal of the information is necessarily condensed, the innovation of a short summary at the end of each chapter, entitled 'First Occurrences and Outstanding Events' facilitates the appreciation of the sequence of events for the reader, and makes the book of very practical use as a work of easy reference. If there is any criticism, it is that it perhaps lives up to its name rather more than some might wish, but the author has stated that his object is to produce a 'short' history, and he is to be congratulated on having accomplished it with no real omissions. In any writing containing concentrated detail of such an extensive subject, brevity is greatly assisted by illustrations, and those depicted by Dr Cianfrani in this book are both helpful and interesting. He has certainly covered a great deal of ground in his search into history for material and pictures, and the result reflects his keen interest in, and enjoyment of, his subject, which will be shared by his readers as whole-heartedly as it is by the writer of this review.

Medizinische Grundlagenforschung
herausgegeben von K Fr Bauer
Band III pp 754 illustrated DM 178
Stuttgart: Georg Thieme Verlag 1960

This useful publication is becoming more international in character, though most of its twenty contributors still come from German universities. As can be seen from the following summary of its contents, this third issue covers a wide variety of topics: modern techniques of psychiatric research; classification of vascular tumours of the brain; muscle tonus from its physiological and clinical aspects; measurements and hazards of ionizing radiations; plasma and other proteins; fructose metabolism; fats and atherosclerosis; lymph flow; blood clotting; synovial membranes; and modern thoughts on Evolution.

The articles vary greatly in length, and their wide range of subject matter make it impossible for any one reviewer to assess their individual merits with equal competence. The production of the volume is excellent, and the index of authors and subject matter add much to its value as a work of reference. In spite of its high price, this work, like its predecessors in this series, should be available in all general medical libraries.

Valvular Disease of the Heart in Old Age
by P D Bedford MD MRCP and F I Caird DM MRCP
pp x+194 illustrated 30s
London: J & A Churchill Ltd 1960

Drs Bedford and Caird have reviewed the literature on heart disease in the elderly against a background of their own experience of 419 patients with valvular disease aged 65 years or over. After an introduction covering sources of data, diagnostic criteria and autopsy observations, subsequent chapters deal with rheumatic heart disease, aortic stenosis, isolated aortic incompetence, syphilitic aortic incompetence, complications of valvular disease in old age, and prognosis. Finally there is an appendix on statistical methods and tables.

This book is a mine of information on the problems of valvular disease in old persons, and although no special methods of investigation have been employed, necropsy data are available on half the patients studied, and the clinical observations are excellently set out, while the life tables are particularly valuable in assessing prognosis.

Many interesting points emerge from this study. Mitral incompetence is more common than stenosis in elderly subjects, and tight mitral stenosis was found in only 14 of 53 patients with rheumatic heart disease, an opening snap being only occasionally heard. It is suggested that mitral valve disease may sometimes develop late in life, rather than in youth, to explain the occurrence of tight stenosis in elderly persons. Isolated aortic incompetence may arise from a combination of senile dilatation of the aorta and a rising blood pressure; atrial fibrillation causes profound deterioration in the clinical status; aortic stenosis (as opposed to sclerosis) is common in old age, its frequency increases with age, and it may develop rapidly in the space of two to five years.

The book is well written, well set out, and the illustrations are clear. There is comprehensive bibliography which covers many aspects of valvular disease not confined to old age. Particularly useful are the comments upon the symptoms of heart disease and heart failure in the elderly, and on anticoagulant therapy.

Only minor criticisms may be made. The table listing the physical signs found in mitral valve disease would have been improved if the cardiac rhythm had been included; the dangers of quinidine treatment are scarcely mentioned, and the use of intravenous hypertonic saline to treat 'water-intoxication' in congestive heart failure might be called in question.

The authors are to be congratulated on this work which should prove of great value in adding to the knowledge of heart disease in old people and to the understanding of the natural history of valvular disease.

Die Okzipitale Dysplasie
by Doz Dr Hermann Schmidt and Dr Erich Fischer
Heft 9 Zwanglose Abhandlungen Aus Dem Gebiet Der Normalen und Pathologischen Anatomie
pp vi+69 illustrated DM 35
Stuttgart: Georg Thieme Verlag 1960

Developmental disorders of the occipital bone and upper cervical vertebræ are far from rare anomalies, and the neurological disturbances that can follow them are sometimes grave. Moreover, the existence of such bony deformities, especially in their less severe forms, may be overlooked clinically, and a misdiagnosis reached whose results may ultimately prove irreparable.

In this short and scholarly monograph from the Radiological Institute of the University of Tubingen, the authors review successively the various anatomical forms and developmental origins of the dysplasias of the occipital bone, the atlas and the axis. In this detailed treatment, they record many linear and angular measurements of the normal bony structures that compose the base of the skull and the upper cervical vertebræ together with those found in the various grades of dysplasia.

Many excellent skiagrams, often accompanied by line drawings to clarify their main features, illustrate the conditions discussed in the text. A list of about two hundred references from the international literature is appended. The monograph should be of considerable service to both neurologists and radiologists.

The Practice of Medicine
edited by Sir John Richardson MVO MA MD FRCP
2nd ed pp viii+973 illustrated 37s 6d
London: J & A Churchill Ltd 1960

The first edition of this textbook for students appeared four years ago. In the interval there have been striking advances in medicine and several of the sections have been re-written. But in spite of this the second edition is shorter than the first. There are 15 authors and in any composite text it is easy to criticize the emphasis and space given to different subjects. In this volume there are thirty pages on venereal diseases but only 22 on the alimentary tract.

The tone is generally didactic. It is arguable whether this is the best approach, although it is still popular with most students. But it might be helpful if the reason for dogmatic statements were given.

Each chapter is followed by a short guide to further reading. These are not, as one might expect, lists of the main papers that the interested student might consult. Only nine of the small total of 73 references are to original papers (and seven of these are in one section); the others are mostly to textbooks. Rather than merely referring to a longer text it would surely be better to guide the student to the classical contributions to a subject, but C M Fletcher is the only contributor to do this. In general British undergraduate textbooks are poor in this respect. Incidentally, the guides to further reading in this volume are very untidy. The date, edition or place of publication of books are sometimes omitted; the same publishers are referred to differently in different sections.

The book is extremely well produced and there are over 60 illustrations. The price is remarkably low.

Carcinoma in Situ of the Uterine Cervix. A Study of 235 cases from the Free Hospital for Women
by Gilbert H Friedell MD, Arthur T Hertig MD and Paul A Younge MD
pp viii+154 illustrated 60s
Springfield, Ill.: Charles C Thomas
Oxford: Blackwell Scientific Publications Ltd 1960

A continuation of a study begun more than thirty years ago by Drs Pemberton and Smith is embodied in this monograph from Boston, Mass. The histological features of carcinoma in situ of the cervix are defined; the microscopical varieties are described in great detail, supported by nearly 100 photomicrographs and it is admitted that the histological diagnosis 'is often not an easy one to make'. Inadequate biopsy and poor conisation specimens lead to difficulties and mistakes in diagnosis. Involvement of endocervical glands by the lesion is recorded in 91% of the cases; if extensive this feature can be difficult to distinguish from invasive carcinoma. The 8 cases from a group of 25 with 'gland involvement and questionable early stromal invasion' in which semi-serial section study revealed microscopic foci of invasive carcinoma were not included in the 235. Vaginal smears and particularly cervical scrapings are needed to support biopsy examination in the detection of carcinoma in situ.

Hysterectomy with or without a vaginal cuff appears to be the appropriate treatment and was carried out in well over half the cases. According to the authors, about 10% of cases are eligible for conservative therapy, implying conservation of reproductive function, but this is a calculated risk. In the whole series treated there was no known recurrence, or development of invasive carcinoma of the cervix.

Nearly all the photomicrographs are easy to read except perhaps Nos 64–67. The publishers have given excellent reproductions of the photographs but the appearance of so much caption

material continued at the foot of the opposite page as on pages 38, 39; 56, 57; 58, 59 may well cause irritation or confusion to the reader. An Appendix containing a well-illustrated description of the Schiller iodone test should be valuable to those unacquainted or as yet unable to utilize it.

Electron Microscopy of the Cardiovascular System An Electron Microscopic Study with Applications to Physiology
by Bruno Kisch MD
translated from the original German text by Arnold I Kisch MD
revised ed pp xii+180 illustrated 60s
Springfield, Ill.: Charles C Thomas
Oxford: Blackwell Scientific Publications Ltd 1960
This small book sets out to show what electron microscopy has so far contributed to the science of cardiology. The author points out that it is really a summary of work up to date rather than a monograph, and it is composed almost entirely of his own research during the past ten years.

A brief introductory chapter on methods is followed by a systematic account of the specialized elements of the heart, the capillaries and the nerve fibres. Much of the text is naturally descriptive and is illustrated by a large number of electron micrographs. Although these are usually of excellent quality, the labelling leaves something to be desired.

In the absence of knowledge of the exact functions of individual structures, the author is to be congratulated on suggestions as to their physiological role. For instance, he has devoted great attention to the number and structure of the sarcosomes, which are very numerous in cardiac muscle and relatively few in skeletal muscle. This may explain why cardiac muscle can work continuously without long periods of rest. The flight muscles of insects also have a large number of sarcosomes, presumably for a similar reason. It is suggested that there is a rich enzyme content of the sarcosomes which may prevent the accumulation of an excess of metabolic products. The author has also found sarcosomes in the endothelium of the capillaries and concludes that the exchange of substances between the blood and the muscle fibres entails much more 'activity' on the part of the endothelium than is generally supposed. He has failed to demonstrate any intercellular cement between the endothelial cells of the capillary wall. So far relatively little work has been carried out on the ultrastructure of cardiac muscle and the author is therefore to be commended on the present account. As additional physiological and biochemical knowledge accumulates, this structural account will gain greatly in importance.

Illustrating Medicine and Surgery
by Margaret C McLarty DAED
pp viii+158 illustrated 37s 6d
Edinburgh & London: E & S Livingstone Ltd 1960
In the Preface the author of this book explains that it was begun eleven years previously, the final result would appear to justify the time spent on it.

Margaret McLarty unlike a number of medical artists approves of the union or integration of the purely graphic with that of the photographic illustration and this is made abundantly clear by the use of a mixture of these in this work. Indeed the author does not scorn to carry a camera on some of her missions to the operating theatres or elsewhere, when the fleeting view or transient phenomenon can be captured by the camera in a fraction of a second, to be translated later into a drawing.

The book is made up of 14 Chapters of 159 pages and contains 178 figures. At first sight this would appear to be a slender number of pages for a large subject, but the subject matter is fully comprehensive and although an occasional repetition obtrudes itself, these lend accentuation to various points.

Important chapters on equipment, lettering and charts will be especially useful to the newly formed department of medical illustration, which is also advised on the essential possession of an electric typewriter. The book is beautifully produced, a shining example of medical art, and the price should ensure a wide sale.

The Case Reports and Autopsy Records of Ambroise Paré
compiled and edited by Wallace B Hamby MD FACS
translated from J P Malgaigne's 'Œuvres Completes d'Ambroise Paré' Paris, 1840
pp xx+214 illustrated 52s
Springfield, Ill.: Charles C Thomas
Oxford: Blackwell Scientific Publications Ltd 1960
Dr Wallace Hamby has done well to collect the case-reports of the great Ambroise Paré, for reading this book is like attending a series of interesting clinical demonstrations. There is scarcely a dull moment from cover to cover of the book.

Ambroise Paré was a wise practitioner, a skilful and resourceful surgeon, and, to judge by some of the reports given here, something of a psychiatrist who in some instances obtained quick results with patients who suffered from obsessions or delusions. Paré even takes himself as a 'case' and describes fully how he directed the treatment of his own compound fracture of the bones of the leg. Though he practised four hundred years ago, there is much to be learnt from him to-day.